FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

(TPSAC)

MONDAY, JANUARY 10, 2011

8:00 a.m. to 5:15 p.m.

FDA White Oak Campus

Building 31, The Great Room

White Oak Conference Center

10903 New Hampshire Avenue

Silver Spring, Maryland

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I N D E X

I N D E X (continued)

P R O C E E D I N G S

Call to Order

DR. SAMET: Good morning. Let's get started. I'm Jon Samet, the chair of the Tobacco Products Scientific Advisory Committee. Good morning to all, and thank you for joining us. I need to make a few statements, and then we'll introduce the committee.

For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues, and that individuals can express their views without interruption. Thus, as a gentle reminder, individuals will be allowed to speak into the record only if recognized by the chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that their conversations about the topic at hand take place in the open forum of the meeting.

We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topic during breaks. Thank you.

Now I'm going to ask Caryn Cohen, the designated federal official, to address the conflict of interest statement.

Conflict of Interest Statement

MS. COHEN: The Food and Drug Administration is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of the industry representatives, all members and non-voting members are special government employees, SGEs, or regular federal employees from other agencies, and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and

conflict of interest laws, covered by, but not limited to, those found at 18 USC Section 208 and Section 712 of the Federal Food, Drug and Cosmetic Act, FD&C Act, is being provided to participants in today's meeting and to the public.

FDA has determined that the members of this committee are in compliance with federal ethics and conflict of interest laws. Under 18 USC Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Under Section 712 of the FD&C Act, Congress has authorized FDA to grant waivers to special government employees and regular federal employees with potential financial conflicts when necessary to afford the committee essential expertise.

Related to the discussions of today's meeting, members of this committee have been screened for potential financial conflicts of interest of

their own, as well as those imputed to them, including those of their spouses or minor children, and, for purposes of 18 USC Section 208, their employers.

These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves receiving an update on the Menthol Subcommittee and receiving and discussing presentations regarding the data requested by the committee at the March 30-31, 2010 meeting of the Tobacco Products Scientific Advisory Committee.

This is a particular matters meeting during which general issues will be discussed. Based on the agenda for today's meeting and all financial interests reported by the committee members, no conflict of interest waivers have been issued in connection with this meeting. To ensure transparency, we encourage all committee members to disclose any public statements that they may have made concerning the issue before the committee.

With respect to FDA'S invited industry representatives, we would like to disclose that Drs. Daniel Heck and John Lauterbach and Mr. Arnold Hamm are participating in the meeting as non-voting industry representatives, acting on behalf of the interest of the tobacco manufacturing industry, the small business tobacco manufacturing industry, and tobacco growers, respectively. Their role at this meeting is to represent these industries in general and not any particular company. Dr. Heck is employed by Lorillard Tobacco Company, Dr. Lauterbach is employed by Lauterbach & Associates, LLC, and Mr. Hamm is retired.

FDA encourages all other participants to advise the committee of any financial relationships they may have with any firms at issue. Thank you.

This morning at 11:00, as requested by President Obama, we will observe a moment of silence to honor the innocent victims of the senseless tragedy in Tucson, Arizona, including those still fighting for their lives. It will be a time for us to come together as a nation in prayer or reflection,

keeping the victims and their families close at heart. That will be at 11:00.

Before we get started, I would like to remind everyone present to please silence your cell phones if you have not already done so. I would also like to identify the FDA's press contacts, Jeffrey Ventura and Tesfa Alexander. And Jeffrey and/or Tesfa, if you're here, could you please stand up?

Thank you.

Introduction of Committee Members

DR. SAMET: Let's proceed with introductions of the committee members, perhaps, Dan, starting with you.

DR. HECK: I'm Dan Heck, principal scientist at the Lorillard Tobacco Company. I'm representing the tobacco industry.

DR. LAUTERBACH: John Lauterbach, Lauterbach & Associates, consultants to the tobacco industry, representing the small business tobacco manufacturers.

MR. HAMM: Arnold Hamm, representing U.S. tobacco growers.

DR. MCAFEE: Tim McAfee, a just-in-time kind of person, here representing the Centers for Disease Control.

DR. BACKINGER: Good morning. Cathy Backinger with the National Cancer Institute, and I'm representing the National Institutes of Health.

DR. WAKEFIELD: I'm Melanie Wakefield. I'm from the Cancer Council of Victoria in Australia, and I'm on the committee representing marketing and communications.

DR. BENOWITZ: Neal Benowitz. I'm Professor of Medicine, University of California San Francisco.

MS. DELEEUW: Karen DeLeeuw. I'm from the Colorado Department of Public Health, and I'm representing government employees.

DR. HATSUKAMI: I'm Dorothy Hatsukami from the University of Minnesota, Professor of Psychiatry.

DR. HENNINGFIELD: Good morning. I'm Jack Henningfield. I work in risk management and health policy at Pinney Associates, and Addiction Sciences at the Johns Hopkins University School of Medicine.

DR. CLANTON: Mark Clanton, Chief Medical

Officer of the High Plains Division of the American Cancer Society, representing pediatrics, public health, and oncology.

FDA Presentation – Menthol Report

DR. HUSTEN: Good morning. I'm Corinne Husten, Senior Medical Advisor with the Center for Tobacco Products at FDA.

DR. ASHLEY: I'm David Ashley. I'm Director of the Office of Science at the Center for Tobacco Products at FDA.

DR. DEYTON: Good morning. Lawrence Deyton, Director of the Center for Tobacco Products.

DR. SAMET: Thank you, and we'll move on with our agenda, the first presentation coming from Corinne.

DR. HUSTEN: Good morning, everyone. I just want to remind everyone that the charge to the committee is to produce a report and recommendations on the impact of menthol cigarettes on public health, including such use among children, African Americans, Hispanics, and other racial and ethnic minorities. The report is due March 23rd of this year.

A brief recap of our previous meetings. Our first meeting in March, there was a summary of the published literature that we had available at that time on menthol, which has since been expanded as we've received information from industry, our own further investigation, and the public; and those articles have been given to the committee for their evaluation.

In June, we had a series of industry presentations. In October, there were presentations on the publicly available industry documents from the Legacy Tobacco Documents Library. In November, there were presentations on the secondary data analyses requested by the committee, as well as marketing data. And at all meetings, there's been information submitted by the public.

Also a reminder, there's a writing subcommittee that's been formed, and that committee has broken itself out into writing groups that are working on the various chapters. I'm not going to list all the chapters, but you will hear information tomorrow from each of the chapters. And the industry

representatives are working on an industry perspective piece as well.

Today, there are several things on the agenda. First, we'll be presenting some information from industry document submissions, the information that can be shared publicly, for some of the questions that have been analyzed. There'll be discussion of a framework of a model to assess the impact of menthol cigarettes on initiation and cessation. We'll have public comments, and then each of the writing groups will have a report about their topics.

Just a reminder that the information presented is for the purpose of helping the committee evaluate the issues and questions and is not a formal dissemination of information by FDA and does not represent agency position or policy.

So, today, we will have some presentations from the industry documents that were submitted. Documents identified by the industry as responsive to questions 3, 4, 8, 9 and 10 have been reviewed under a contract from CTP. Analyses of the rest of the

documents is ongoing, and some of that will be presented at a later date.

Our FDA review of the summaries has determined that some of the information is commercial, confidential, or trade secret. That information will be provided to the TPSAC SGEs in closed session, but the information that can be shared publicly and is not deemed commercial, confidential, or trade secret will be presented at today's meeting; however, that information that can be presented publicly is limited.

TPSAC had also asked for models of the impact of menthol cigarettes on initiation and cessation, and Dr. Mendez is developing such a model under contract by FDA, and the framework will be presented today to get input from the committee. And as requested by FDA at the last meeting, each of the writing groups will be presenting.

As many of you know, Dr. Connolly recently resigned from the Tobacco Products Scientific Advisory Committee. As an internationally renowned expert on tobacco control and the prevention of

tobacco-related diseases, he brought valuable expertise to the committee. We've really appreciated his hard work, his perspective, and his commitment to the issue, and we wish him well in all of his future endeavors. This resignation will not impact the timing of the report -- it's still due in March -- and we are in the process of selecting a replacement.

Today we have several questions for the committee. The first is, what suggestions does the TPSAC have regarding the proposed model that will be presented; what suggestions does the TPSAC have regarding the general approach to the review of the evidence that's been discussed at earlier meetings; what suggestions does the TPSAC have regarding the strength of evidence criteria, again discussed at earlier meetings; and, then, what suggestions does the TPSAC have regarding the approach outlined by each of the chapter writing groups?

Are there any clarifying questions?

[No response.]

DR. SAMET: I guess not. Thank you.

Then we'll move on to the presentation by

Dr. David Mendez from the University of Michigan, School of Public Health. We've asked David to provide guidance to the committee and develop a model that may allow us to make estimates of the public health impact of various scenarios related to the presence of menthol cigarettes.

David has begun work on this modeling framework. I think this is the first time that the committee has heard from David on this topic, although we've had discussions about the general idea of using models in approaching our charge.

Just to say by way of introduction, David has a long history of working on modeling of public health impact, both of tobacco, radon, and other factors that affect public health. So thank you for joining us.

Menthol Modeling Schema

DR. MENDEZ: Thank you and good morning. My name is David Mendez from the University of Michigan. I'm going to discuss the building of a model to assess the population dynamics of menthol cigarettes. The model is based on a compartmental model that we

have developed at the University of Michigan. And, essentially, what we do is a model of adult smoking, adult cigarette smoking, and it just combines just policy, different policy scenarios in terms of initiation and cessation rate. Those are what you see at the left. Then it keeps track by age, sex, and smoking status, former, never, current smokers, and then compares the survival rates under different scenarios to compute benefits, costs, and associated prevalence under the different policies. So within the model, we keep track of former smokers, again, by years quit, as well as age and sex.

So the model in general follows a tank model, so there's initiation at one end and cessation, and the prevalence is the remaining -- the volume of the tank. So we keep track of that. We have used the model -- this is just general. We have used the model to forecast and predict general prevalence for adult smoking prevalence in the U.S., and the model has done quite well. And we have also used the model for different policy scenarios; what would happen with prevalence if we don't do anything; what would

happen with prevalence, for example, if we adopt measures that will take initiation and cessation like we have in California, for example. So we have done this kind of analysis.

We also have done analysis with a model predicting what would be the prevalence in the U.S. if we input some policies on initiation and cessation gradually that will diminish initiation or increase cessation at certain levels.

These are some of the potential inputs and outputs of the model so we can keep track of the prevalence by smoking status; current smoker, former, and never smokers, and by age group. And the bottom graph represents, one -- the prevalence on the right side represents the inputs that we can -- the change of parameters we can put in the model. This is just an example of the way that this model can be characterized. So these are other examples of output that we get from the model, undiscounted smoking-related death and life years lost, et cetera.

Now, what particularly I would like to discuss is how to -- I am modifying the model to take

into account the issue at hand, which is the prevalence of menthol cigarettes.

So the model is going to again be -- it's a compartmental model that keeps track of individuals by age, sex, and smoking status. And smoking status are former, never, and current smokers, and the former smokers by years quit. And the following parameters are -- so we have the children here, people less than 18 years old, and we have the parameters that -- you know, the birth rate of the population. At age 18 -- it's not that all the initiation happens at age 18, but we are concentrating initiation at age 18, and after that, everything is cessation.

At age 18, we have a proportion of 18-year-olds that become smokers and the proportion that are not going to be smokers are never-smokers. Then that proportion of people 18 years old that become smokers, then we have a proportion of them that are going to become menthol smokers. And then they are going to progress here to the menthol current smokers, and here there's no menthol current smokers.

There's a transition between these two categories, between menthol and non-menthol. So there's a possibility of switching at different ages. And then there's some cessation that can be differential for menthol and non-menthol smokers, and they're going to become former smokers here. And then, of course, the latest stage is death, and we have all the necessary -- need to get all the necessary death dates for this.

So the green parameters are the parameters that we already have incorporated in the model. The ones that are red are the ones that I need input from the committee to see what are the ranges of those parameters and figure out what kind of sensitivity analysis we need to do, whether we have data for those parameters or what are the ratings for sensitivity analysis.

So the proportion of smokers of 18 years old that will become menthol smokers is one of them. The probability of switching from menthol to non-menthol and vice versa is another one. And then the quit rate for menthol smokers is another one. And, of

course, we have death rate for menthol, if there's any differentiation between the death rate for menthol and non-menthol. Of course, this is not just -- the model accepts not the possibility of one parameter, but that the parameter can change in time and with age.

So the idea is, then, just we should be able, with a model like this, to put some changes in the parameters and changes in initiations, differential changes in initiation and cessation because of policies and figure out at the end what is the difference between the policies that we are examining versus the status quo or the counter-factual that there's no menthol smoking.

So I'm open for comments and questions.

DR. SAMET: Thank you, David. That was a quick overview of a fairly complicated activity, so I would anticipate that we will have questions. And I think your guidance on where we will need to interact with you, I think, is important.

Neal?

DR. BENOWITZ: Have you got the capacity to

segment by racial/ethnic groups? Because that's going to be an important thing, because there may be different behaviors by different racial/ethnic groups. Have you got the substrate to be able to do that?

DR. MENDEZ: Yes, we do.

DR. SAMET: Yes, Melanie?

DR. WAKEFIELD: So in the section on 18-year-old smoking initiation and menthol initiation, those kind of -- whatever they are -- shapes there --

DR. MENDEZ: Here?

DR. WAKEFIELD: Yes. The other ones. So this, though, does it have a capacity -- I'm not saying there's evidence for this, but presumably a model should entertain the possibility that there might be, that if menthol wasn't available, a young person wouldn't start.

So here they've got an option to choose menthol or not menthol and go into becoming a current smoker, by the look of it.

DR. MENDEZ: Oh, yes. That's --

DR. WAKEFIELD: Where does --

DR. MENDEZ: No. That's actually a very good observation. So I have separated the two parameters, initiation rates. So, overall, initiation rate 18 years old is about 21.4 percent right now. And then after that, there's some proportion of them that become menthol smokers.

So suppose that we don't have -- so the question is, suppose that we don't have menthol smokers; then we need to change that initiation rate. So they are coupled. That's why they are -- I set up two parameters that should be somewhat correlated. So if one changes, so the other one, then I'll need some input about how that will affect the other one. But absolutely, that has to be --

DR. SAMET: Corinne?

DR. HUSTEN: Since African Americans initiate smoking, on average, one or two years later than whites, I guess it's a similar question, whether 18 is the best age for truncating initiation.

DR. MENDEZ: That's something that is easily changed. So I will welcome the input of the committee on that because that's something we can

change very easily.

DR. SAMET: Neal?

DR. BENOWITZ: I also had a question about duration of smoking. It looks like in this model that a smoker is translated to certain death rates. Do you have part of this model that can incorporate how long a person continues smoking a particular kind of cigarette? So if that's different, that should impact death rate or disease rate.

Is that part of the model?

DR. MENDEZ: The model assumes that initiation starts at roughly age 18. And when they quit, they quit, and that's the duration of the smoke. So we are not tracking individual people, but we are tracking groups of people. So the idea is that -- so we have a flow of individuals that started at a certain age.

So we keep track of every single cohort and start 18 years old, and then 19, 20. And then there's a proportion of 20-year-olds that quit, a proportion of 30-year-olds that quit every year. And then when they quit at 30 or they quit at 35 or they

quit at 40, the time that they smoke is the time, 35 minus 18, when they started smoking. And then they follow the curve from there of former smokers.

DR. BENOWITZ: I understand that part. But I'm just wondering, it looks like it's just a single arrow that goes from current smoking to, say, death rate or disease rate. Is that arrow modified by how long they were a smoker?

DR. MENDEZ: Yes.

DR. SAMET: And David, if I understand, you're using -- the relative risk values are CPS?

DR. MENDEZ: CPS2.

DR. SAMET: CPS2. So that's where they're coming from.

Dorothy?

DR. HATSUKAMI: I was wondering how your model might account for moderating factors in addition to ethnic/racial groups. There are higher problems of menthol smoking among the individuals that are lower SES as well.

So the question is that these individuals who are at lower SES may also have less access to

healthcare, which might influence their cessation rates. So does your model account or help us understand those influences as well?

DR. MENDEZ: As it is right now, no. But what you're asking me is can it be desegregated into more compartments, and the answer is yes, very easily. We just need to know how many compartments are important in order to determine what you need.

DR. SAMET: Maybe in follow-up, Dorothy -- and again, if this is something that comes from the menthol group, that it might be appropriate to model a group, let's say, with less likelihood of quitting than the population in general, I think what we would need to do is work with David to construct such populations.

Mark?

DR. CLANTON: I think there's an overall trend in the comments and questions that we may end up needing to run the model a couple or three times, maybe, for different groups. For example, we may need to run the model for the overall population and see what comes out in terms of death rates of menthol

versus non-menthol. But, clearly, in terms of African Americans -- and you've heard this already -- there's going to be a different factor applied to the switch rates between menthol and non-menthol cigarettes. In fact, relatively few in the older age groups are going to switch from menthol to non-mentholated cigarettes.

So it appears to me we may solve this problem by modifying the model based on what Jon just said, what we want to see. But we may end up running this model two, three, four times, and then looking at those numbers and comparing them to each other based on the groups we're looking at. I don't think one model is going to solve or answer all of our questions.

DR. SAMET: I think what the model will do is give us the tool to carry out multiple sensitivity analyses. I was actually thinking we weren't going to run two, three, or four times; perhaps 2-, 3-, or 400 times; probably more realistic is different scenarios.

I just want to remind everyone that David

told us that in the boxes here are various parameters for which he would need us to make estimates. Some of these are the focus of the various writing groups; for example, the question of what cessation rates are in menthol versus non-menthol smokers and so on.

So these are -- the target of reviews where we're looking for the best answer or what the range of best answer supported by the literature is, again, opening up the possibility of sensitivity analyses around those ranges of estimates. And this overall figure corresponds in concept to the figure, I think, that was originally put together last July. So I think it's quite consistent with the way we've been conceptualizing the approach to the problem and the use of models.

Other questions? Yes, Tim?

DR. MCAFEE: I apologize for not being able to look at you while I use the microphone here.

I have two questions. The first is really a follow-up on Melanie's initial question, which is just wanting to be sure that the -- because if you look strictly at the flow diagram of how the model is

working, it looks like you're saying that everybody -- - in order to become a current non-menthol or menthol smoker, you have to pass through menthol initiation. And obviously, that's not --

DR. MENDEZ: Menthol initiation means that it's a decision; do you start menthol or not? So that's -- you don't have to --

DR. MCAFEE: It's a yes/no on that.

DR. MENDEZ: It's a yes/no.

DR. MCAFEE: Right. But sort of related to that, I guess what I'm struggling to think about is how this model -- you're going to set up a bunch of parameters and estimates for what the various rates and proportions are for this. But the ultimate question that we're trying to answer is what will happen if we make a radical alteration in the current situation, i.e., we take -- as one possibility. What would happen if menthol was not an option either for initiation or for continuation? And at that point, presumably, things are going to -- that's really a separate question from describing the current situation. So I'm just curious how the model will

deal with that.

DR. MENDEZ: Well, yes. That's part of the parameters. So the parameters will change for that scenario. So we are going to model the current scenario, but then there's another set of parameters assessed, or let's take menthol out of the picture, and then let's estimate what would be the initiation if menthol would be out of the picture, and then run the model again and compare the two scenarios.

DR. MCAFEE: Right. So for instance, at menthol initiation, at that point, we're not just going to assume that everybody who was going to menthol, current smokers, is now going to never smokers. We're going to have to come up with estimates --

DR. MENDEZ: Exactly.

DR. MCAFEE: -- as to what will then happen, where people will go.

DR. MENDEZ: Or a range of estimates so we can do some sensitivity analysis.

DR. MCAFEE: Thank you.

DR. SAMET: Yes, Mark?

DR. CLANTON: We just realized that this is really a classic decision analysis diagram as opposed to a flow diagram. So on one hand, it helps us understand how this works as a decision analysis. On the other hand, it's pretty easy to modify this. It looks like we can drop in other decision points pretty easily into the model and modify it pretty easily. But it made sense to me once I figured out it's a decision analysis.

DR. SAMET: I would note that there's been a lot of this kind of work done in looking at tobacco control and tobacco control scenarios. And if I remember correctly, it's a recent issue of the American Journal of Public Health --

DR. MENDEZ: Yes.

DR. SAMET: How recent? November or what?

DR. MENDEZ: Well, it was July.

DR. SAMET: July. So the July 2010 issue of the American Journal of Public Health has an editorial by David, discussions by others, about the use of models. And there was a, I think, 2006 issue of the American Journal of Public Health on modeling,

and then there's an NCI monograph as well. So there's a fairly rich background of references for those wanting to catch up on this area.

Let's see. Anything else? Any other questions? Yes, Dorothy?

DR. HATSUKAMI: Since I'm leading the chapter that is relevant to this decision-making model, what kind of information do you need to plug in the numbers for this model? Do you have to do a meta-analysis of some sort to take a look at, for example, cessation rates between menthol and non-menthol? I guess I want to get a clearer idea of what information's going to be very critical for you.

DR. MENDEZ: Well, the information critical for me is the information, the parameters, that are set in red here. So I would like either ranges or point estimates or ranges of parameters for those specific -- for example, I would like to know what proportion of initiation is menthol. I would like to know also what is the probability of switching from menthol to non-menthol. Does that change with age? Does that change for different ethnic groups? Does

it change by sex?

The more desegregated the information is, the more accurate the model is going to be. We can aggregate as much as is necessary, given the information, but then we have to run more sensitivity analyses.

DR. SAMET: But I think, Dorothy, to further amplify it, I think what David will be looking for is the TPSAC estimates of these parameters and their ranges so that he can then use them in his model. So these would be forthcoming from the literature review.

Just to remind everyone, I think the most frightening thing I've heard today was March 23rd. And that means that if we're going to interact with David and have useful results coming from his analyses that can be incorporated into our report, we would need to be giving him our views of what these various parameters are on a relatively short-term basis, that meaning, I think, probably the next roughly three or four weeks, because I think it would be important for us as a committee to sit, then, and

look at the results of the models and see if this will be useful for incorporation into the full report, in part to fulfill our mandate to look at impact.

So, again, I think we know we're on a short time frame. We're fortunate that David was able to step up and help. I think one clear message, and I think this goes back to what Mark and others have said, is that to fulfill our charge, we will need to have racial/ethnic group and perhaps other population-specific models developed. And I think we probably can give you some very quick guidance on that following this meeting.

Anything else?

[No response.]

DR. SAMET: Good. Well, thank you very much for your presentation, and we look forward to continuing to work with you.

Let's see. Now, remarkably, we started late, but we are on time for a quick 15-minute break while we get ready for the next segment. So we'll take a 15-minute break. Committee members, remember, no

discussion of the meeting topics during the break amongst yourselves or with any member of the audience. And we'll start again at 9:15. Thank you.

(Whereupon, a recess was taken.)

DR. SAMET: We're now going to move to a series of presentations related to requests on submissions related to menthol, the first of these by Richard O'Connor from Roswell Park Cancer Institute, Dose-Related Interactions Between Menthol and Nicotine. Rich?

Dose-Related Interactions between Menthol and Nicotine – Richard O'Connor

DR. O'CONNOR: Can everyone hear me? Can everyone hear me?

DR. SAMET: Yes, we can.

DR. O'CONNOR: Great. So as Dr. Samet said, the topic that I was assigned was Dose-Related Interactions between Menthol and Nicotine on Consumer Perceptions of Nicotine Strength and Uptake and Metabolism of Nicotine.

So by way of notes and disclaimers, although the work reported was done under contract with the

Center for Tobacco Products at FDA, the content and conclusions of this presentation are my own.

So the purpose of this analysis was to inform TPSAC about the contents of documents that were submitted by manufacturers pursuant to FDA requests on this topic. And the topic, in particular, is interactions between nicotine and menthol vis-a-vis consumer protection of nicotine strength, as well as metabolism of nicotine.

So in terms of the documents that were submitted, there were 96 documents submitted that were responsive to topic 4, and this totaled 1,342 pages in total. Now, FDA's preliminary evaluation has determined that these documents contain commercial confidential information, and so the information contained in those documents will not be presented in the open session. But I can say, in summary, that it appears from the documents that were reviewed that little internal industry research has been completed that directly addresses these issues. But this limited evidence that was there will be submitted to presentation to the TPSAC SGEs in a

closed session.

So that concludes my very brief presentation.

DR. SAMET: Okay. We'd be surprised if we have questions, but this committee has surprised me before. Neal?

DR. BENOWITZ: Neal Benowitz, Richard. Are there any documents that you looked at that were not reviewed by the work of Greg Connolly?

DR. O'CONNOR: I can't say that I'm familiar exactly with exactly what documents Dr. Connolly reviewed, so I would have to go back and look and try and do a match-up.

DR. SAMET: Corinne?

DR. HUSTEN: Any documents that we've been able to ascertain are available in a public forum, like a legacy database would no longer be commercial confidential and would be presented at the meeting. So this was in response to the letter asking the industry to submit documents. We have attempted to search to see if any of them are out there in any kind of public format such that they could be presented. In this set, we did not find any of them.

DR. BENOWITZ: So just to be clear, this analysis excludes the ones that Connolly has published on?

DR. HUSTEN: This is the sum total of what we got that was analyzed, and nothing within what was identified as being responsive to this question, we were not able to find any of that in the public domain on our initial search. Now, we're continuing to do more, and if we find some of it that is in the public domain, we'll come back and present that in an open meeting. But our initial search did not find anything that's in a public forum.

DR. BENOWITZ: So I'm beginning to understand. Since Greg has published a lot on this, then those documents should have been part of this review, and those are in the public domain. So I don't understand why they weren't included.

DR. HUSTEN: All we know is what we got and what we're able to find.

DR. SAMET: Jack?

DR. HENNINGFIELD: I think this came in part from questions of a number of us that concerned how

dosing selection was made for menthol, not just the interaction between menthol and nicotine. And what I'm wondering is, are there other analyses that are going on; will we see anything that gives us any information about the selection of menthol dosing, regardless of whether it has been studied for how it interacts with menthol.

In other words, as I think I stated at one meeting, I assume that the industry just doesn't take menthol and pour it in. There has to be some predetermined specification for what the dose of menthol is in a menthol cigarette as well as in a cigarette that contains menthol but is not branded as a menthol, regardless of whether a nicotine/menthol interaction has been studied.

Are we going to get any information on that?

DR. HUSTEN: Some of the information that you're referring to is in questions 13 to 16. That's been deemed to be commercial confidential, and will be presented in closed session, so around doses of menthol in menthol cigarettes versus those that are not defined as menthol cigarettes.

DR. HENNINGFIELD: Maybe I missed that. But the closed session, will we be getting that in this meeting?

DR. HUSTEN: Not in this meeting, no. We'll be presenting to the various writing groups, where it's relevant, and then in the closed meeting in February, they'll be presented to the full TPSAC.

DR. SAMET: Anything else?

[No response.]

DR. SAMET: Then we'll move on to the next presentation by Hernan Navarro from RTI, impact of menthol on the neurobiology of tobacco dependence.

Impact of Menthol on the Neurobiology of Tobacco Dependence – Hernan Navarro

DR. NAVARRO: Good morning.

DR. SAMET: Hi. We can hear you okay.

DR. NAVARRO: Good. I'm presenting on topic 3. I'll go through the disclaimers that this presentation is to inform TPSAC regarding the impact of menthol cigarettes on public health, and any opinions that I render during this presentation reflect those of RTI and not the FDA.

So topic 3, the impact of menthol on the neurobiology of tobacco dependence, we took that to mean, does menthol change the pharmacodynamics of nicotine, that is, the way nicotine works in the body, or does it have a direct or a modulatory effect on the neurotransmitter pathways associated with reward? So when we reviewed the documents that were submitted by industry, we looked for information that addressed these two questions.

The approach we took, there were three documents that were submitted that were a total of 108 pages, and each document was reviewed by two researchers.

The types of -- hello?

DR. SAMET: We're okay.

DR. NAVARRO: Okay, because I heard some beeps there.

The types of documents that were reviewed, there were internal reviews of published literature and industry data on the use of menthol as a tobacco flavorant. And we received two documents. They were duplicates, one dated April or July of 2002, and the

review covered -- it was just an extensive review of menthol and included such things as the physical and chemical properties, the pharmacokinetics and toxicology of the compound.

There was one other document -- it was a concept document -- that recommended investigating the effects of menthol on the levels of nicotine and cotinine, but there was no indication if the recommendation was acted upon.

The findings and summary, none of the information in the documents directly addressed topic 3. Much of the information in the internal reviews was published in a paper by Heck in 2010, and the conclusion of that review was that menthol did not appear to affect the pharmacokinetics of nicotine. And that ends my presentation on topic 3.

DR. SAMET: Thank you.

Let me ask if there are committee questions. Yes, Neal?

DR. BENOWITZ: Since much of the work has been published by Dr. Heck, can you talk about what is not available? I think we've all seen Dr. Heck's

paper, but I'm just curious to know what's not in there.

DR. SAMET: Dan, please.

DR. HECK: Yes. That paper was a review of published literature. There was some previously unpublished information in there, but that was just smoke chemistry and some in vitro and in vivo biology attached as appendices. So all of the text was peer-reviewed published work, no unpublished industry work.

DR. BENOWITZ: Again, what was the nature of the work that was not finally published by you? Because I'm curious to know -- I've read your paper that has been published, but I haven't read the paper that's not published.

DR. HECK: Oh, I see. The one referred to here, that was just simply an earlier version of that same review paper text that I updated and then published.

Does that answer your question? The 2002 work referred to here?

DR. BENOWITZ: The comment was made that much

was published. I'm just wondering about the rest of it that wasn't published. What sort of information was that that was not published?

DR. HECK: None that I'm aware of personally.

DR. SAMET: Corinne?

DR. HUSTEN: I'm probably not the best person to answer this question, but I think there was information on a variety of topics, and some of the information not related to nicotine. I think all of -- I mean, the conclusion was the conclusion that was put up there around nicotine.

DR. NAVARRO: Yes. When I read the internal documents, there was some industry data in there. And when I read the review, I wasn't sure if -- I mean, I was not able to pick out each piece of industry data. So I felt it safer just to say that much of the information was in that review instead of all.

DR. HECK: Yes. I apologize. I'm not recalling the specifics from that 2002 manuscript. It is available on the Web. My recollection was it was all published work that was reviewed, but there

could have been some internal work in there. I just don't recall at this time.

DR. SAMET: Other questions?

[No response.]

DR. SAMET: Then let's move on to the next presentation, James Hersey from RTI International, Comparative Rates of Initiation.

Comparative Rates of Inflation – James Hersey

DR. HERSEY: Thank you. Delighted to be here. What we did was review industry documents related to topic 9, Comparative Rates of Initiation for Menthol and Non-Menthol Cigarettes. We did this work under contract for FDA, but this is our work, not yet vetted by or approved by FDA.

We were looking at comparative rates of initiation on documents as identified by the industry. When we did our review, we were looking for characteristics of menthol and non-menthol smokers. We were looking for information on the age gradient, on uptake of menthol versus non-menthol cigarettes and trends in smoking. And we really were focused on information that could help identify the

role of menthol cigarettes on initiation and uptake of smoking.

We reviewed, I think, 87 documents, about 2500 pages. Each document was reviewed by a pair of researchers. And then if you look at the abstracts we created, we've done one which was, this is what the industry said, and if we had any comments, those are from us. Those are separated out.

In terms of the documents by volume, most of what we received were a succession of various versions. There's some PowerPoints and the associated computer output, with a presentation, parts of which have been shared with this panel by the industry earlier on underage use of menthol cigarettes, a use involving re-analysis of the National Household Survey on Drug Use and Health.

There are also some analyses of where do kids purchase cigarettes from YRBS. There were a few non-data documents, a description of a proposed market segmentation study from 1997, a couple unpublished literature reviews of public literature. And there were a few data industry studies which we won't talk

about today.

In terms of trends in menthol and non-menthol cigarette use, one of the industry documents found when they looked at NSDUH data between 2002 and 2008 was that the decline in the prevalence of smoking among 12- to 17-year-olds was primarily among the number of people who smoked non-menthol cigarettes, and that the proportion or number of youth who were smoking menthol cigarettes was fairly constant.

Also, between 2002 and '08, there was an increase in proportion of youth smokers who were smoking Marlboro Menthol; that increased from like 10 percent to 16 percent of sales of youth who were smoking those cigarettes, and also a big increase in the sales of Camel Menthol during that same time period, from 2 percent to 6 percent of youth reported smoking that kind of cigarette.

Again, this is illustrated from a graph taken from that report. The top line shows a change in the proportion of youth who report smoking Marlboro, regular Marlboro cigarettes. So non-menthol cigarettes, in terms of proportion, are going down.

On the other hand, the second solid line, which was from Newport Menthol, remains fairly constant over time. The third straight line down is showing the increase in Marlboro Menthol cigarettes, which, again, is moving up in that time period, up to about 20 percent. And then the bottom straight line was showing the increase from about 2 percent to 6 percent in the proportion of youth who were using Camel Menthol cigarettes during that time period.

The documents spoke a lot about age gradient, which means menthol smoking is more common among younger than among older smokers. One of the things I found different from my earlier study was that in 2008, the proportion of menthol users actually wasn't any -- was not higher among newer rather than more experienced smokers. I'll return to that in a second.

Nonetheless, there was a pretty strong age gradient. So the proportion of smokers using menthol was like 45 percent among 12- to 17-year-olds, then drops to 39 percent of 18- to 25-year-olds, then drops to about 30 percent of older smokers.

One of the new facts that we learned was this age gradient, as menthol cigarettes are more popular among younger smokers, remains constant even when you control for the length of smoking, which they did in this analysis.

So among people who'd smoked less than 100 cigarettes, 43 percent of 12- to 17-year-olds were smoking menthol cigarettes versus 37 percent of people 18 to 25. That finding was also true among people who'd smoked more than 100 cigarettes, again more common among younger smokers, 12- to 17-year-olds, than people 18 to 25.

Similarly, even among people who had, say, started smoking in the last two years, if you were 12 to 17, half of the 12- to 17-year-old smokers who started in the last two years were smoking menthol cigarettes, compared to about 40 percent of people who are 18 to 25.

The one difference on this trend was among people who -- youth who had started smoking within the last year. That number was a little bit higher by proportion among 18- to 25-year-olds. And the

reason for that appears to be influenced by the fact that this limited recognition of -- a lot of young people don't know what kind of cigarettes they were smoking, whether they're menthol or non-menthol. The industry document shows that 18.5 percent of 12- to 17-year-olds who started smoking in the prior year did not know whether they were smoking menthol cigarettes or not. One caveat is these data from the 2008 NSDUH data, that that was a lower year for menthol use and some other ones, so we need to monitor these as we move forward.

Implications for all of this is that the decline in menthol use in cigarette use is primary among non-menthol cigarettes rather than menthol cigarettes. There's been an increase in percentage of youth smoking some popular menthol brands over the last decade. And one can think about menthol as a starter product -- I mean, menthol cigarettes in 12- to 17-year-olds wasn't high. While it wasn't higher among people who just started, it was much higher among 12- to 17-year-olds than older age groups, and this trend was constant even when you controlled for

the length of smoking. And a lot of youth really do not recognize that they're smoking menthol cigarettes.

Thank you.

DR. SAMET: Thank you. For clarification, this percentage of the respondents not reporting what product they smoke --

DR. HERSEY: Yes.

DR. SAMET: -- did you comment on a change in that prevalence over time?

DR. HERSEY: The change in that prevalence was not reported in the document that I reviewed.

DR. SAMET: Okay. Thank you.

Neal?

DR. BENOWITZ: I've got two questions. The first one is, in this very last slide, you have some very interesting data about the age gradient among underage smokers, saying that there's a greater percentage among smokers who start at age 12 to 13 versus 14 to 16. But you didn't present any data.

DR. HERSEY: I can find that for you.

DR. BENOWITZ: Yes. I think that would be

very interesting to see that.

The other question that I have is if you go back to the figure where you looked at different brands over time --

DR. HERSEY: Yes.

DR. BENOWITZ: -- and it looks like there are changes in youth among some month brands, but not all menthol brands.

DR. HERSEY: Yes.

DR. BENOWITZ: For example, Newport didn't.

DR. HERSEY: Newport remains -- Newport was a high brand and remained fairly high.

DR. BENOWITZ: All right. So my question is, do the differences in trends -- are they the same among adult smokers versus youth smokers?

DR. HERSEY: Those data were not reported in the document I reviewed.

DR. BENOWITZ: Because I think it would be interesting to see if the brand trends were the same among adult smokers compared to youth smokers.

DR. HERSEY: Yes.

DR. SAMET: Jack?

DR. HENNINGFIELD: Another question on the changes in brands, was any of that explained or related to different ethnic groups picking up different brands? For example, there was a large increase in Marlboro Menthol. How did the ethnicity of the Marlboro 18 percent users compare to the --

DR. HERSEY: Well, while that's analyzable, it was not reported in the documents that I reviewed. So I can't answer that right now.

DR. SAMET: Arnold?

MR. HAMM: On your page number 7, where you have the menthol brands listed, you have Marlboro regular and then Marlboro Menthol, then you have Newport Menthol and Newport regular. What is Newport regular?

DR. HERSEY: That was what was in the document, so I suspect Newport had introduced -- so I don't know the answer -- from the documents I reviewed.

MR. HAMM: Thank you.

DR. SAMET: Other questions? Actually, Corinne, let me ask a question to you just about what

further we may or may not see around the submissions. In other words, we're seeing these slide presentations. Will there be written reports? Or if one of the writing groups, for one reason or another, wanted to go back to the actual submitted documents, how would we do that? So what are next steps here?

DR. HUSTEN: Well, again, any of the commercial confidential information, which you're not seeing today, will be presented in closed session. Some of it is -- like, for example, this was a graph that was directly in the documents. And so the review is constrained by what was submitted. And so in a case like this -- I mean, this is what it was, and so it was just provided. But if you have questions about things where you would like to ask if there's more detail, just ask us and then we can ask RTI to take a look and see if there's any expansion on any of it.

DR. SAMET: Yes, Cathy?

DR. BACKINGER: Just a quick question for clarification. I'm assuming this is true, but just want to confirm it, that the documents that you

reviewed did not include any breakdown by race/ethnicity.

DR. HERSEY: None of the documents on that topic that I saw reviewed data by race/ethnicity, at least that I recall. I could look again.

DR. SAMET: Jack?

DR. HENNINGFIELD: I guess I'm still wondering if we're going to get information that will help us understand which sub-populations account for some of the changes. And the Marlboro Menthol is just fascinating because it's going from 10 percent, thereabouts, to equaling Newport, and on a trajectory to exceed it as a dominant menthol brand.

Is that reaching the same populations? Is it reaching new populations? Is it reaching populations of kids that never would have -- that would have been unlikely to have smoked at all? Is there any information that you've seen or that we will see that bears on that?

DR. HERSEY: I believe that could be analyzed. I didn't see that in the documents that I reviewed.

DR. SAMET: Okay. Thank you very much.

So we'll move on to our next presenter, Eric Johnson from RTI, rates of switching.

Rates of Switching – Eric Johnson

DR. JOHNSON: Well, good morning. This work was conducted by myself, Scott Novak, and Jennifer Schoden. And we're reviewing the rates of switching to and from menthol and non-menthol cigarettes. That's topic 8. As has been stated in several other presentations, the views and analyses reflected in these slides are those belonging to me and to RTI, and not to the FDA.

The purpose of our work here is to review the provided industry documents on rates of switching between menthol and non-menthol cigarettes, and, if possible, to infer whether the switching between flavors of cigarettes plays any role in recent initiators adopting regular smoking or current smokers maintaining smoking in the face of adverse stimuli or respiratory disease symptoms.

A little bit of background. As far as we could find, there are no published studies of rates

of switching specifically between menthol and non-menthol cigarettes. However, studies of brand loyalty suggest relatively limited switching in general, and, specifically, menthol cigarette smokers may be less likely to switch, at least in response to price increases; that is, it's been found that they're more likely to use discount coupons and to switch, actually, to higher tar and nicotine content menthol cigarettes in response to price increases. And in a recent analysis that was published in December in Addiction, they estimated that about half the number of menthol smokers would switch, compared to non-menthol smokers, in response to a projected 10 percent price increase.

Nonetheless, there is indirect evidence that menthol and non-menthol switching may play a role as a starter cigarette, then switching to non-menthol cigarettes later, given the general prevalence of smoking menthol and non-menthol in the population; and also that they may help maintain smoking in the face of these adverse effects.

Also, there have been prior analyses of

public industry documents made public suggesting that menthol/non-menthol switching may have some effect on -- or has been altered. The dosing of menthol levels have been changed to appeal to individuals that are intolerant of the harshness and irritation of non-menthol cigarettes.

So we did a content analysis, each of the documents reviewed by two independent sources, characterizing the content of those on a variety of parameters. We reviewed all of the information, abstracted it, and categorized documents as useful; that is, they directly said something about switching between menthol and non-menthol, those that we could infer some information about switching based on brand analysis, and those that were not useful at all.

So we reviewed 37 documents, a little over 1300 pages. Two of the documents were excluded, one because it was a duplicate of another document, and another because it was simply a memo indicating that they had no relevant information.

So we reviewed 35 documents, and I'll begin to characterize the documents that we were looking

at. One thing to note is that much of the information that we reviewed was from the 1990s. There were a few documents in the early 2000s and very few in the past five years.

The kinds of documents that we looked at, many of them were survey reports or data tables, and these were just documents with sets of data tables, no text or information about where the data came from or necessarily even what they represented other than what was in the table, some memos, slides, and bulleted lists.

Many of the documents, even the survey reports, did not provide the study methods that went into developing the percentages that were reported, and, therefore, provided no real context for the data we were looking at. We didn't necessarily know how the folks who responded to the survey were sampled or how the estimates may have been weighted or weren't weighted for complex sampling design, et cetera.

The sources of information that were reported, where we could tell; these were cigarette tracking surveys, call-in surveys where they included

a request to participate in a survey in a cigarette pack or something like that, and also national or market-area-based telephone surveys. All the documents that discussed age indicated that they were talking about adult smokers, 18 and older.

Collectively, the documents that we reviewed were really focusing on marketing studies. So they were focused on brand-switching behavior, losses, gains, opportunities, market share, and didn't necessarily specifically address issues around menthol versus non-menthol; oftentimes not breaking out, for example, Marlboro Menthol versus Marlboro.

So overall, 19 of the documents contained no useful information, 7 provided some indirect evidence about menthol and non-menthol, and 9 were actually useful.

One thing I should mention before we look at the data on switching specifically, switching in this context, at least where it was documented, was really looking at regular smokers, people who had smoked for more than a year, who had changed brand in the past 12 months, and they described it as "packing,"

really. So it could be length, it could be flavor, it could be a variety of things. And I've noted the packing definition here, filter, non-filter, and so on. And this is just a reminder at the bottom that we are presenting what's considered publicly available data or non-commercially confidential data.

This is the first -- well, switching in general is, of course, a behavior that includes things other than menthol/non-menthol. And what this slide represents is data from the switching book that dates from 1991 that Philip Morris produced, and talks about rates of switching overall, so any sort of packing switching occurring. And you can see we have a high of 14 percent, a low of 7, and a rebound, if you will, to approximately 9 percent in 1991. So, overall, there seem to be some significant minority of cigarette smokers that are switching brands on a year-to-year basis, at least from 1981 to 1991.

Some corroborating evidence from a different report, a different study, is the Menthol Market Study Fact Book. And this slide shows the length of time that smokers have been smoking their current

brand or their most-often-smoked cigarette. This does not distinguish new smokers from regular smokers who switch, so we can see that between 4 and up to maybe 9 percent may have switched in the past, switched to a new brand, but we don't know exactly what that would be.

Again, from the switching book from Philip Morris, this slide shows the overall rates of switching, combining the 1990 to 1991 data. And so this is among all current smokers, the rate of switching, so approximately 9 percent. Again, I'll remind you that we don't really know exactly how the percentages were calculated, and there are no confidence intervals in the document. While I've put this into our own graphic, these numbers are exactly what was in the document provided.

Just as an orientation, we have switching from menthol and non-menthol cigarettes, and then switching to. And the particular interest of this presentation is the cross-switching, switching from menthol to non-menthol, and from non-menthol to menthol. And you can see that that accounts for

about half a percent of all current smokers. Bear in mind, this is not among switchers.

They also broke out this same rate by variety of demographic characteristics. And so, again, this repeats the overall sample, which is a 34,000-member sample, and we see the same rates of switching that we saw before, overall. And you see here that, to some extent, women have -- if you add these up, because these rates are among women and among men and ages and so on; that there's somewhat greater switching among women than men, as well as, at least for the switching from non-menthol to one of these others, menthol or non-menthol, it's a little higher it appears, in younger age groups, 18 to 24, than in older. We also see some trend overall in the cross-switching, that is, from non-menthol to menthol, in this column, and switching from menthol to non-menthol, again where it's somewhat higher in the younger age groups, 18 to 24, than in the older.

This is a percentage we could find looking at menthol/non-menthol switching among switchers. Okay? So among all the 9 percent that switched in that 1990

to 1991 time frame, about 8 percent were switching from non-menthol to menthol, while 26 percent switched from menthol to non-menthol; so quite a bit larger in one direction than another.

They also provided the same sort of breakdown in terms of demographic characteristics and the percentage of switching among switchers. Again, we see somewhat greater switching among women, particularly those switching who are formerly smoking menthol and smoking either non-menthol or menthol or their current brand.

We see somewhat less of a trend with regard to age, particularly when we're looking at the menthol cigarettes and switching away to non-menthol. They don't account for as large a proportion of the smokers as they did when we were looking at the rates overall. But we do see this sort of cross-switching trend higher among younger adults than older adults when we go from non-menthol to menthol.

Also of potential interest, when we look at switching among African Americans or the racial or ethnicity breakdown among switchers, there is a

concentration of switching for African Americans who are switching -- even when they were smoking non-menthol, they account for a larger percentage when they're switching to menthol cigarettes as their current brand. And that's true whether they are originally non-menthol smokers or menthol smokers. So they're reflecting or switching to the overall trends that you see in the population as a whole.

Some other interesting information that we can talk about today that is somewhat relevant to switching, and this isn't necessarily switching entire packs, but smoking menthol and non-menthol as a mix. We see that the reasons given by smokers for smoking menthols appear to differ between exclusively menthol smokers and primary non-menthol smokers.

The exclusive menthol smokers primarily mention taste as a reason for smoking menthol, and a relatively small proportion, 6 percent, mention some health concerns as a reason for smoking menthol cigarettes. In contrast, those who primarily smoke non-menthol cigarettes but occasionally smoke menthol cigarettes, the reason for their smoking menthol

cigarettes given, they had a lower endorsement or mentions of taste but a much higher mention of health concerns.

So, in conclusion, the submitted tobacco industry documents provide limited useful information. Most of it is marketing-focused on brand-specific analysis, so we couldn't really look at rates of menthol/non-menthol switching per se. They had very limited description of the methods that went into producing those prevalence rates. And the material that we could really look at numbers on is pretty dated.

But nonetheless, overall, brand switching occurs fairly -- or appears to occur fairly regularly in smokers as a whole, but it's relatively limited when we look at cross-flavor switching. About half a percent of current smokers switched from non-menthol to menthol or from menthol to non-menthol in the one estimate that we have of that. And among switchers, again, it's a significant minority of switchers that switch between flavors, and most of it, or a larger percentage of it, is from menthol to non-menthol.

I included the references from the background section, and that's my contact information if you need it. Thank you.

DR. SAMET: Thank you.

Mark?

DR. CLANTON: Thank you for your presentation. On the definition of switching, is that an industry-based definition or was that provided by the researchers who were doing this analysis?

DR. JOHNSON: That was provided in the primary document that we reviewed here, the switching book. So it's an industry-provided definition.

DR. CLANTON: Yes. I was a little confused by the definition. I assume you're looking for, or whoever created the definition is looking for point prevalence in a particular year of switching.

DR. JOHNSON: Right.

DR. CLANTON: Because as you read this, if someone was smoking for two years, and in the beginning of year three they switched to menthol, they would not be counted as a switcher based on this

definition. So I was trying to understand how that worked.

DR. JOHNSON: Right. It depends on when they were ascertained. If they were ascertained in the year that they had switched, they would be considered a switcher. And one of the things that they were trying to distinguish, in contrast with the second slide that showed the length of time someone had been smoking a particular brand, they were distinguishing switchers from new smokers. And so, yes, they were oriented to this past-12-month time frame.

DR. BENOWITZ: Could you go back to conclusions number 2?

DR. JOHNSON: I will, yes.

DR. BENOWITZ: I don't understand the last two bullets. If the estimates of past year rates are very similar for the second-to-last bullet, and then the last bullet is looking at all past year switchers, it would seem to me, since the population of non-menthol smokers is much greater, that, if anything, the absolute proportion among switchers should be the other way around. There should be a

greater number of non-menthol going to menthol.

So where does this last bullet come from? Where do these numbers come from? I don't understand. They seem inconsistent.

DR. JOHNSON: Well, actually, I guess the rate of switching is the same -- that's the rate of switching not among -- the first bullet is the rate of switching among all smokers. Right?

DR. BENOWITZ: Right.

DR. JOHNSON: And then this is the rate among all switchers. And so the menthol switchers account for a greater amount of switching.

DR. BENOWITZ: Yes. It seems --

DR. JOHNSON: As far as -- also I will put the caveat out there that these are the numbers we derived from their tables. We didn't calculate these at all.

DR. BENOWITZ: Right. But what I don't understand, since there are more non-menthol smokers in general, and since .5 percent are switching, you would think that that figure would be much greater among the percentage of all switchers.

DR. JOHNSON: Yes. They're switching, but they're not switching to menthol.

DR. BENOWITZ: No, no, no. It says non-menthol to menthol.

DR. JOHNSON: No. I mean, the balance of those non-menthol switchers are switching to another non-menthol cigarette.

DR. BENOWITZ: No, no. At the top, you said non-menthol to menthol is .5 percent of all smokers.

DR. JOHNSON: Right.

DR. BENOWITZ: Menthol to non-menthol is .6 percent.

DR. JOHNSON: Right.

DR. BENOWITZ: Well, there are more non-menthol smokers in the population in general.

DR. JOHNSON: Sure.

DR. BENOWITZ: So you'd think that the absolute number would be greater for non-menthol to menthol. And then if you were to look among switchers, since the absolute number is greater, then the percentage of switchers should be greater. So I just don't -- it doesn't make any sense to me. I

don't understand how you calculated the bottom two lines.

DR. JOHNSON: I didn't calculate it. But we can double-check the numbers that we got from -- I mean, I know they're accurate to their tables. We can double-check what they did to generate those numbers to the extent possible.

DR. BENOWITZ: Yes. I think it's important because, to me, it just -- unless I'm really missing something, the mathematics don't add up.

DR. SAMET: The non-menthol to menthol, that's of non-menthol switchers, 7.7 percent switched to menthol and 92 point --

DR. JOHNSON: '90-'91.

DR. SAMET: What? I'm not --

DR. JOHNSON: Combined years 1990 to 1991, they -- I mean, they're reporting a behavior that occurred in the past 12 months.

DR. SAMET: Right. But the 7.7 percent is of all non-menthol switchers, 7.7 percent --

DR. JOHNSON: Right.

DR. SAMET: And 92.3 percent stayed with a

menthol brand.

DR. JOHNSON: Correct. Stayed with a non-menthol.

DR. SAMET: Just to make clear that we're all interpreting that as you think it should be interpreted.

DR. JOHNSON: Uh-huh.

DR. BENOWITZ: And I've got a second question. When you talk about reasons for smoking menthol, was that analyzed separately by people who were lifelong menthol smokers versus switchers?

DR. JOHNSON: No.

DR. BENOWITZ: Because I think it would be interesting.

DR. JOHNSON: They distinguished what they call exclusive menthol smokers versus people who didn't always smoke menthols. And it could have been some time in the -- I mean, they occasionally smoke menthol or they may have smoked them in the past and have switched.

DR. BENOWITZ: I think it would be interesting for the committee if there were any data

on switchers versus people who were exclusively menthol for the long term to try to find out why people are switching.

DR. SAMET: So one other question. The switching book, is it a book? How long is this?

DR. JOHNSON: It's fairly long. I forget exactly, but it's probably 100 pages or so.

DR. SAMET: I mean, again, the reason I ask is a lot of questions have come up, and you're giving us a very selective look, by the nature of it. And, again, this may be a document, actually, that perhaps one of the subgroups, writing subgroups, would want to see, primarily for its own review.

DR. JOHNSON: Right.

DR. SAMET: I mean, I think, again, if we were to use any of these materials in our writing, I think we actually -- Corinne, just make a note, we really do have to have them in our possession to use them.

DR. JOHNSON: Sure. Correct. And the vast majority of the book just isn't relevant to menthol/non-menthol.

DR. SAMET: Sure. Understand. Thank you.

Jack?

DR. HENNINGFIELD: I want to pursue this a little bit because understanding who is switching and why is of great potential public health import. And I'm assuming that you and others have prepared reports that in the process of that, you may have learned things that maybe were beyond the scope of your charge. So my question will be to push you a little bit.

For example, if menthol could contribute to the population prevalence of smoking, which has been, let's say in adults, roughly stalled for a few years, it could contribute to that stalling by delaying cessation, by being a place to go for people who would have otherwise likely quit. If we can understand, are there subpopulations that would have been likely to quit but they switched to menthol instead, that's of great public health significance. I'm wondering if you have seen data that would be relevant to understanding that.

Also, and I think this is related to Dr.

Benowitz' question, if menthol was serving as an initiation product or category for young people that may have been unlikely to have begun smoking, but then they switched away from menthol, even though people are switching away from it as they grow older, it still may have had its worst public health impact by recruiting people. And I think this is what I'm trying to understand, to help understand the public health impact of menthol.

DR. JOHNSON: Well, in answer to your first question, we may be able to discuss that in the closed session because there's some information that may be relevant there, but I can't discuss it here.

With regard to your second question, there really is nothing that we found that is specific to initiation per se and switching. We'd hoped to find something, but we did not.

DR. SAMET: Cathy?

DR. BACKINGER: Back to the percentage of switching among switchers with the 7.7 and the 26.1, do you have the sample size or the end for that? Because I guess that was maybe getting a little bit

at what Neal was asking.

DR. JOHNSON: Right. Right.

DR. BACKINGER: And you just presented the percentages, and it would be --

DR. JOHNSON: Sure.

DR. BACKINGER: Realizing it's not a nationally representative sample, per se, but just what the sample sizes were.

DR. JOHNSON: Right. Yes. Well, I'd have to go back and look. I don't recall off the top of my head what the ends were for that particular table. I'm not even sure that they were given. But we could probably calculate them.

DR. BACKINGER: I think that would be helpful. Thank you.

DR. SAMET: Other questions?

[No response.]

DR. SAMET: Thank you.

We'll move on, then, to the presentation by Andy Hyland from Roswell Park Cancer Institute, Rates of Cessation. Andy?

Rates of Cessation – Andrew Hyland

DR. HYLAND: Thank you again. My name is Andy Hyland, in the Department of Health Behavior at Roswell Park Cancer Institute in Buffalo, New York. I'll be reporting on the documents that I reviewed as part of the process here related to question number 10, which is looking at rates of cessation, smoking cessation, among menthol smokers and non-menthol smokers. The disclaimer, although the work reported here was done under contract with Center for Tobacco Products at FDA, the content and conclusion of this presentation are mine. And, again, my goal here is to share what we digested out of the documents that were relevant to question 10, quitting, menthol smokers and non-menthol use.

The document analysis, a point I want to make is that the document coding is based solely on the industry's classification as to being relevant to this particular question. There were 48 documents that were noted as such in the submission to the Center for Tobacco Products across all the companies that were asked to provide information. There were 48 documents, for a total of 283 pages. Five of

those documents were deemed to be informative. Three documents were reviews of the published literature that's publicly available. Two documents summarized the results of an industry study looking at this issue. Forty-three of those 48 documents were deemed uninformative or not relevant. Thirty-eight of them were output files from a statistical package without any context or code book or an unknown data set. And five of the documents were deemed not relevant to the specific question.

The one industry study that I mentioned that was summarized in two of the documents I looked at, it was a cross-sectional study that looked at indicators of nicotine dependence as measured from the Fagerström Test for Nicotine Dependence and time to first cigarette, comparing that between menthol smokers and non-menthol smokers. And in one of the documents, they reported that there was no statistical association between menthol status of the smokers and either the FTND or time to first cigarette. And the second document was a very similar presentation of these data, but just the data

on FTND were reported and not the time to first cigarette.

So from this particular study, it was overall data. The results were not stratified by race/ethnicity, for example. But the conclusions from these two documents, menthol smokers do not have increased risks of nicotine dependence compared to non-menthol smokers.

The three documents that were reviewed that were industry reviews of the published peer-reviewed literature, of the three documents, there were really two separate reviews. Two of the documents were linked, and I'll share the summary of those findings here.

The first review focused just on cessation, so really looking at tobacco users and then looking at the subsequent quit rates, either in a prospective manner or in a retrospective manner. There were 14 studies that were included in this review. Six were categorized as no effect, and the studies here are listed as how they were classified in this particular document. So six studies, no effect. Six studies

categorized as mixed results, and two studies were categorized as potential poor cessation outcomes.

The conclusion from this particular document is, "Results reported to date are mixed. While some studies have yielded results consistent with the view that menthol cigarette smoking affects cessation, the vast majority have produced null or mixed results." And it goes on. "As a result, it is currently not clear whether smoking menthol cigarettes leads to poorer cessation outcomes or whether those outcomes are the product of other confounding factors." So that's one review.

The second review was very similar in some ways but was more extensive in another. This document looked not only at cessation but also indicators of nicotine dependence among those who continue to smoke.

The cessation component of this document reviewed 16 studies. Eight were coded as no effect, three were categorized as mixed results, three categorized as potential poorer cessation outcomes, and two were coded as indeterminate. And the

particular studies that are referenced are noted here. So that's looking at cessation.

Then the component of this document that looked at nicotine dependence among smokers of menthol and non-menthol products, 12 studies were included. Seven were categorized as having no effect, two categorized as no effect but noted with a question mark in the document; one was noted that menthol smokers have less dependence, and two noted that menthol smokers have greater dependence.

The summary conclusion here is the industry review categorized most studies as showing no effect or mixed results. However, there do exist studies that show menthol decreases quitting or increases dependence.

So the summary of the findings, or my synthesis of these documents, just five documents were deemed relevant to this particular topic. The one industry study that examined this did not find any significant associations between menthol and dependence or cessation -- actually, dependence. The industry study just looked at the association between

menthol and dependence.

The industry's review of the published literature led to a mixed results conclusion on whether menthol cigarettes make it more difficult for smokers to quit. And that's my prepared remarks. I'd be happy to take any questions.

DR. SAMET: Thank you. Just a quick question. The literature review that you mentioned, does this have any author attribution or is it simply a report?

DR. HYLAND: Just a report.

DR. SAMET: Dorothy?

DR. HATSUKAMI: Andy, in the literature review on dependence, did they differentiate how dependence was measured?

DR. HYLAND: The industry study?

DR. HATSUKAMI: Yes, the industry study.

DR. HYLAND: Yes. The FTND were put into tertiles, perhaps, and I'm trying to recall from the -- so the scoring of the FTND was in there, and time to first cigarette, I think, was coded, dichotomized, at 30 minutes, if I'm recalling correctly.

DR. HATSUKAMI: But they didn't do an analysis by the dependence measure; they just lumped it all in.

DR. HYLAND: No. In this particular document, it was just overall findings. No results stratified by, say, indicators of nicotine dependence, race, ethnicity, socioeconomic status. Just overall results were reported.

DR. HATSUKAMI: And that was true for the cessation information as well? There was no categorization by race of ethnicity?

DR. HYLAND: Correct. The cessation -- in the industry study, they really only could look at nicotine dependence because the study were all smokers and they were reporting on the levels of dependence. The cessation, the piece in these documents that really looks at cessation really was solely just a review of the existing published literature. So some studies report things broken out by various factors; others don't. None of that was summarized in these particular documents, although one could do that by going to the source documents

and pulling it out.

DR. HENNINGFIELD: I have a comment and a question. The comment is I just want to make sure I've got my own understanding, if it's consistent with yours, because on one hand, your conclusion from the industry is that menthol does not reliably increase dependence, but it appears that when there is an observed effect, it is in the direction of increasing dependence and not decreasing dependence.

Is that a fair summary?

DR. HYLAND: Let's take a look here. So, for example, these are the data from this particular study -- the one review, 12 studies, six no effect, six mixed, two poorer outcomes. Yes. There's just -- it's either no effect or pointed toward menthol being associated with greater levels of dependence or poorer cessation outcomes in those few, relatively few, studies that do find a significant association.

DR. HENNINGFIELD: So my summary is not unreasonable, that when there is an effect observed, it's in the direction of increasing and not decreasing dependence?

DR. HYLAND: Dependence. Correct. That's my interpretation from these.

DR. HENNINGFIELD: And the other thing that is a comment and just a reminder, that the way we end up with people at a certain dependence level is a combination of, does the substance, the act, the manipulation, whatever, in this case menthol, increase the risk of dependence; and among those who become dependent, does it increase the level of dependence. And your focus is on level of dependence, not whether or not it contributes to risk of dependence.

DR. HYLAND: Correct.

DR. SAMET: Neal?

DR. BENOWITZ: Did you try to do any analysis of the source data, like for the total exposure study?

DR. HYLAND: The information that would permit one to do that analysis was not provided in the documents that we reviewed, that were sent to the Center for Tobacco Products.

DR. BENOWITZ: Corinne, is that something

that is planned to be done by FDA, or is there some way that we can request some analysis of those data?

DR. HUSTEN: There's the potential -- I think the main problem is time in terms of being able to get you something from the total exposure study in a period of time that would allow you to assimilate and incorporate it into the results. FDA does intend to look at the data in terms of our continued thinking about this issue.

DR. BENOWITZ: Because I --

DR. HUSTEN: It is limited, to some extent, in terms of measures and stuff. We do have information about the questions that are in there, and we could provide that to you.

DR. BENOWITZ: Because, as many people have brought up before, it looks like the overall documents don't really segment by race/ethnicity. But I assume that the total exposure data set does have that information, and I think it will be important to look at that question.

DR. HUSTEN: It has information. We can give you, I guess, the set of questions that are in there

so that you can see if there are measures that you think are particularly interesting.

DR. BENOWITZ: I think another issue, which is important, is when you look at dependence, with the FTND, it's looking at cigarettes per day. But when you're going across race/ethnicity, we know that that's a problem because African Americans, on average, smoke cigarettes more intensively than Caucasians. So I think the FTND is limited, and we need to explore other dependence measures.

DR. SAMET: Dan?

DR. HECK: Yes. I don't know with precision exactly what papers or the internal study on Fagerström was referred to here. I have a sense that this is the study that was presented at the SRNT meeting last year by the authors. And so, if someone has more interest in the way the Fagerström is analyzed, they might look at that pollster presentation.

I note also that we did -- Jack noted we do see some mixed findings for some of the studies. Just a reminder that these studies where we've seen

those mixed findings with regard to cessation are clinical studies of cessation therapies where the menthol variable was probed in the secondary analysis. So I think there may be reasons why some of those studies' findings were different than those of the large smoker population in the total exposure study.

DR. SAMET: Mark?

DR. CLANTON: Was there any data that allowed you to look at numbers of cigarettes smoked per day and sort of reflect that against, again, the dependence outcomes?

DR. HYLAND: Not summarized in these data here, although, presumably, if source data from, say, the total exposure study were available, that could be done. And the other approach in the published literature that was reviewed, there's data sets associated, and some of those analyses may be incorporated. So that could be undertaken.

DR. CLANTON: I think that might be helpful because there's this question about why -- if you smoke a lot of menthol cigarettes, that you may not

have this relationship between first cigarette smoked and nicotine dependence. But in a recent study, it basically said there may be a sweet spot. In other words, people who smoke 6 to 10 cigarettes per day seem to have to have that cigarette earlier than others. However, if it goes above 10, 10, 20, or more, then that relationship sort of disappears, looking at time to first cigarette.

So if we look at some of those mixed studies as it relates to numbers of cigarettes and see if the sweet spot of 6 to 10 comes up again, again, there is a publication, a recent publication, that brings that out.

DR. SAMET: Other questions for Andy?

[No response.]

DR. SAMET: Thank you.

So looking at our agenda, we're doing well. We have time for committee discussion; in fact, we have a lot of time for committee discussion. And I think this, in theory, committee discussion, relevant to the presentations that we've just heard, of course, raise a number of issues that are critical.

So I suggest that we take time for further discussion, as needed, on what we just heard on these issues, on the presentations, which I think in general pointed to -- aside from the pending commercial confidential presentations -- relatively limited literature, but a few potentially informative documents for our purposes.

Melanie?

DR. WAKEFIELD: I suppose one question that we probably all have is when will we hear this commercial and confidence information, because it would be really helpful to hear it sooner rather than later as we are writing our chapters.

DR. HUSTEN: We agree, and we are trying to get those scheduled via call and Adobe Connect. So I'd encourage you, when Caryn calls you, to try to get dates to try to be available. We're going to try to provide alternate dates to give everybody a chance to work with their schedule, but we are trying to get them scheduled as soon as we can.

DR. SAMET: Jack? Oh, sorry.

DR. WAKEFIELD: Do you intend to do it

chapter by chapter, or are you going to try to get everyone on the line?

DR. HUSTEN: Well, some of the questions are more directly relevant to some chapters than others, but some of it's going to depend on how hard it is to get people's schedules.

DR. SAMET: Jack?

DR. HENNINGFIELD: I have questions on each of the topics, but I'd prefer right now to just go back to the first one, which was more related to menthol interactions with nicotine and dose-related interactions. And what I'm still trying to find out is, irrespective of specific nicotine dose-related interactions, what is the basis for dose selection of menthol by the industry? That's what I'm still trying to understand.

I'm not sure if we'll get more of this in closed session. But if you think about it, it's not credible that the industry determines menthol concentrations capriciously or without some kind of foundation. They have to make decisions as to what level of menthol to put in a non-menthol branded

cigarette; should the level be changed in the light version of that cigarette; should it be changed to compete with a competitor?

What is the foundation evidence? There's got to be some evidence, some data, that the industry has. And we've been asking for it and haven't seen anything like it.

Are we going to get anything like that?

DR. HUSTEN: Well, I think the questions that you're referring to are questions 14 and 15 of the questions that were submitted to industry. Question 14 talks about some products are not marketed as menthol but may contain menthol and identifying the threshold at which you identify and market a product by reference to menthol flavoring. And then 15 is the rationale for adding menthol. Those were considered commercial confidential, and as we get the calls scheduled, we will be presenting those data. And then they will be presented in the closed session in February.

DR. SAMET: Dan?

DR. HECK: I would remind the committee we

did see, at least in a general sense, some of that information presented in the July briefings. We saw information on the menthol levels in some major brands extending back some decades, and those levels having been stable. Frankly, those levels were established in the circa-'70s era before a lot of the mechanistic information on menthol was precisely known. So I think it might best be described as traditional levels that were instituted at those times.

With regard to the rationale or reason for different menthol levels in lighter-yielding cigarettes, cigarettes particularly containing a lot of tip ventilation, we heard a little information on that as well. There are practical reasons why menthol loadings are slightly higher in cigarettes of low-yield design. However, we also saw information that the resulting smoke menthol levels are not necessarily higher, as a reflection of the way the dilution and filter efficiency is higher on those cigarettes. It affects the ratio, the relative amount of menthol delivered in the smoke relative to

that supplied.

So there is some information on that, broad brush, at least, and perhaps some of the trade secret information will provide some detail on the specifics.

DR. SAMET: Other general comments? Neal?

DR. BENOWITZ: It's not a comment to this, but I just want to ask FDA something because I'm not sure what format to do it in.

When I was reading through some of the documents that talked about menthol, it was stated that in some cigarette brands, there were other things like peppermint and spearmint oils that were added. Are those banned now or are those other potential things that could still be added to menthol cigarettes?

Can someone tell me about that?

DR. HUSTEN: What's been banned are cigarettes with characterizing flavors that are candy sweet, spice. So there's nothing that says substances can't be added to cigarettes if it's not a characterizing flavor.

DR. BENOWITZ: So can we find out if some menthol cigarettes also contain peppermint and spearmint now as part of the flavoring?

DR. HUSTEN: There may be some information in some of the documents that will be presented in the closed session that may be helpful.

DR. BENOWITZ: I think it's important because if we're talking about sensory effects, I think that those flavorings would be important.

DR. HUSTEN: I mean, you have to realize that the questions that were submitted to industry were those from the March meeting and did not specifically ask about those flavorants.

DR. SAMET: Jack?

DR. HENNINGFIELD: A broader question raised by Neal's question, though, that I think we need to keep in mind is the definition of menthol. Is it reliably a single molecule, a single isomer of a single molecule, or can menthol perception be altered by, say, holding that molecule constant and adding a little bit of a molecule defined as peppermint?

Is it reliable? I don't know. But that also

gets to the issue of what would you do about menthol and how would you define -- how would you categorize the action that you were going to take. Would it be everything based on a single molecule?

DR. SAMET: Dan?

DR. HECK: Yes. I think perhaps to Jack's and Neal's comments both, the confidential information that you may be reviewing will speak to this. But my offhand sense is that the quantities of L-menthol, which is the cooling principal in the peppermint plant and the one that has the primary cooling properties, the levels contained or added, due to other flavors that may contain L-menthol as a natural constituent, are really trivial compared to the levels applied as such in a menthol cigarette. So I think you'll see that these levels are substantially lower.

DR. HENNINGFIELD: A follow-up to that: So is menthol added across all companies? Is it the naturally-occurring mixture of L and D-menthol, or is it purified? Is it mainly the L that's added, or how does that compare to what is naturally occurring in

peppermint oil?

DR. HECK: The L isomer is the naturally occurring form. The D isomer generally has a mustier taste and it's used mainly for topical products like shaving creams and things like that. It has less utility as a flavor.

Both the natural plant-derived botanical-sourced L-menthol, which is essentially 99-plus percent, quite pure, with some minor fractions from the natural peppermint plant, is used, as well as synthetic menthol that, again, is 99-plus percent L-menthol. So both are used commercially in both foods and confections and in tobacco products.

DR. BENOWITZ: Can I just ask a follow-up? Are there some products that are particularly enriched with D-menthol as a way to change the taste characteristics?

DR. HECK: Not that I'm aware of. Just my personal knowledge, I'm not aware of that. But my understanding is because of the musty note, D-menthol or racemic mixtures mainly find use in topical preparations, not for flavor use.

DR. SAMET: Cathy?

DR. BACKINGER: I'm going back to Dr. Hyland's presentation, and that he received or they received 38 reports that were deemed uninformative because they were raw SPSs, output files, without any context. So I guess I'm thinking that the tobacco industry submitted those because it was in response to a specific question, and so they felt that it was relevant. And I'm wondering – and, again, it may be a running out of time issue for the report. But will FDA ask industry the context of those output files and whether there are any code books or what the data sets are? Because, again, we may run out of time, but I'm just wondering. Like they submitted it because they felt it was responsive, but Dr. Hyland and his group couldn't analyze them because there was no context or code book.

DR. HUSTEN: Yes. And in the request, we had requested -- I'm trying to find it here, because I believe that was part of the request, was the relevant -- so we did ask for scientific protocols, design features. And we asked that the documents be

submitted in a file format and structured format that allows for meaningful review, accompanied by name and version of the software, name and definitions of variables, copies of programs and macros, and other things. But the analyses are restricted to what we received.

DR. BACKINGER: Right. But it sounds like that perhaps -- and I'm just interpreting what you just said, is that they provided these output files because they felt it was relevant, but they didn't provide all the information for anyone to actually analyze the data, which is what you asked for. Again, I don't know if the plan would be to go back and ask for clarification.

DR. HUSTEN: Well, these were mandatory submissions, and presumably we received everything they have.

DR. SAMET: Neal?

DR. BENOWITZ: I've got a question for FDA or industry. We received some documents about compounds that are not menthol but work like menthol. They work on the same receptors. They're sort of

artificial menthol.

Do we know anything about whether they are in any cigarettes?

DR. HECK: Well, I know that -- I think the Leffingwell website was provided to us here as a good way to at least get an introduction to that literature. There are about I think around a thousand compounds known to flavor and sensory sciences that have some cooling properties. Only a relative handful have broad utility as flavors. And I think there may be a few of those on various industry usage lists. I don't know for sure, but I would imagine that because the cooling sense that's communicated by menthol is not certainly unique to menthol. You know, cineole, eucalyptol, -- there are a number of other natural botanical constituents that have some cooling properties.

DR. BENOWITZ: I think it would be important -- if we are looking at the menthol issue, we're really looking not just at menthol but things that are like menthol as well. It will be important for us to know about that, more about what's in

cigarettes.

DR. HUSTEN: Again, you gave us the questions, and we submitted those questions to industry. So you will not get any other information unless the industry just provides it as part of the public comments because we would have to go back and do another request, and there's a certain procedure for that, including OMB review. So it's nothing you're going to get by March.

I mean, if there are things that you would like us to take into account as we continue our review after the report's completed, please let us know.

DR. BENOWITZ: Well, I would just ask that when you're reviewing all the documents you're reviewing, if you see anything, let us know.

DR. HUSTEN: Okay.

DR. SAMET: Jack?

DR. HENNINGFIELD: I agree with this point. And without starting new investigations, maybe those that have been already looking at documents may have seen documents concerning other substances. And this

gets to the issue that I raised earlier, is everything about menthol defined by one molecule, or in fact menthol is a term that is sometimes used when other parts of the peppermint oil extract are used as well as that molecule. That's really important. Otherwise we could be focusing on just one part of the problem.

DR. SAMET: Other questions? Tim?

DR. MCAFEE: Well, this is on a different topic. It's actually going back to the presentation by Dr. Hersey on topic number 9 on the rates of initiation for menthol and non-menthol cigarettes. I apologize for not having noted this during the time of the presentation. But on page 8 of that, it stated that a review of the NSDUH 2008 results that menthol cigarette smoking in 12- to 17-year-olds was not higher in newer than more experienced smokers; and the second bullet, that started in the past year, it was 33 percent; started in the prior two years, was 50.5 percent.

I just was noting one of the other documents in our presentation packet had reviewed the NSDUH

study that was published by SAMHSA in 2009, which essentially reports exactly the opposite relationship with smokers who began smoking, that in the past 12 months had rates of -- if they began smoking -- so less than a year versus more than a year was 44 percent, for less than a year, and 32 percent.

So I'm just curious, perhaps, of trying to double-check on why we're getting two different reports on what would seem to be potentially an important question in terms of the pathway of initiation, not totally critical in and of itself since we have all the other information about the increase in the age categories themselves. But nonetheless it caught my eye initially when I saw this, and then when I see something that's saying exactly the opposite, we should try to figure out why.

DR. SAMET: Let's see. Other comments? We're running ahead of schedule. That's okay. Jack?

DR. HENNINGFIELD: On the same topic of initiation, this topic goes to the really big public health question, which is the potential impact of

menthol on undermining prevention programs and, conversely, contributing to initiation.

The Marlboro Menthol is a fascinating case history that I think we need to understand better because it was going up so dramatically, from 10 to 18 percent, and we don't know where it will end up. But right now it's on a trajectory to exceed what has for years been the dominant menthol brand.

So the big question is, is that rise just cannibalizing other cigarette selection or other Marlboro regular, in which case, maybe, from a public health perspective, it's relatively neutral? Or is that rise contributing to initiation of smoking among young people who may not otherwise have started smoking at all? And if that's the case, then that's a very serious adverse public health effect. But it's a fascinating experiment to go from 10 to 18 percent in what? Was that roughly 10 years?

DR. SAMET: Yes.

DR. HENNINGFIELD: I think understanding that has some pretty serious implication for understanding the nature of the problem and what to do about it.

DR. MCAFEE: Just one quick follow-up on Jack's point. I think there was some evidence presented that would suggest that it wasn't just brand-switching or cannibalization in the same report that it was reported that the decline in smoking prevalence of 12- to 17-year-olds in that six-year period was primarily in the number who smoked non-menthol cigarettes rather than menthol cigarettes. So it appears that either the menthol brand was more robust at initiation than non-menthol brands or that there was something about the menthol characteristics that was keeping kids from non-initiation.

DR. SAMET: Other discussion by the committee at this point? Corinne?

DR. HUSTEN: Related to the question about other flavors, in the request to industry, we had said the term menthol includes menthol derived from both natural and synthetic sources as well as menthol analogs and functional equivalents.

DR. BENOWITZ: So, as I said, did you get anything about functional equivalents?

DR. HUSTEN: Well, I have to leave it to the

questions that were presented today, if there was anything in those documents. As I mentioned, there may be something in some of the documents that you'll get in closed sessions. But I can't speak to the five questions that were presented today, if there was anything in there about other mint-type flavors.

DR. HECK: We heard some previous discussion of the WS series of compounds that are noted cooling compounds of considerable potency beyond that of menthol, even, which is the normal reference compound. I know there's been research into those. But we'll see what's disclosed, but I'm unaware of it ever having been translated into a commercial product.

DR. SAMET: Mark?

DR. CLANTON: Dan, are you aware of any sort of competitive activity or inhibition at the receptor sites for menthol, of menthol analogs? In other words, do those things compete for the same physical space on the receptors or are there multiple other receptors that seem to be affected more by analogs as opposed to D- or L-menthol?

DR. HECK: I think in terms of the WS compounds, WS23 and cousins, they do bind the TRPM8 receptor, the thermal/cold receptor by which we feel cold. There's a little crosstalk with the irritant receptors as well, the 1A1, I believe it is, which is why menthol also has this kind of unpleasant, irritating sense, too, at certain levels. While it's pleasantly cooling at lower levels, it has unpleasant sensory properties at higher levels.

So I think our knowledge of all the sensory receptors that are at play here, and, as you may know, the hot pepper receptor is of a related class. So we have the extremes of thermal/cold and noxious heat and noxious chemical irritation, all a very closely-related family of receptors.

I'm sorry. I don't recall the original question.

DR. CLANTON: Well, it sounds like, based on your answer, that given the family of receptors, analogs may actually have their own -- affects more receptors than others as opposed to them all competing with L- and D-menthol for the same space on

a particular receptor. It sounds like a variety of receptors can be activated for chemosensory effects as opposed to multiple molecules fighting to get on one receptor.

DR. HECK: Yes, I think so. But the WS compounds, anyway, the fairly new generation recently grasped for food use, structures that are noted for their cooling potency, are, I think, relatively specific for the TRPM8 receptor.

DR. SAMET: Corinne, I think this question is for you. When we do hear the commercial confidential, about the commercial confidential materials, if there are aspects of those materials that we feel are relevant to our report, how would they be discussed or considered or included or mentioned?

DR. HUSTEN: An extremely good question because commercial confidential information cannot be discussed in public or put in a public report. And so I think if there are things that you think you would like to say, we would need to run those by our FOIA people to see if they cross a line in terms of -

- certainly you wouldn't be able to quote them or cite them specifically; whether you can talk about them in general terms, we would have to see what you want to say and then see if you can say that.

DR. SAMET: Okay. Well, I think this will be important for us to hear these presentations on a relatively timely basis because if there's anything that we view as important there and we need to decide and learn, I guess, in a sense how to use it, we'll all be operating on a very short time frame, obviously.

DR. HUSTEN: Yes. And that's why we're very anxious to get those calls scheduled. So, again, if you can accommodate your schedule at all, we'd appreciate it.

DR. SAMET: I'm sure we can.

Jack?

DR. HENNINGFIELD: I want to just make an observation on how we look at the data related to dependence or addiction because this is the field that I live in primarily. And you can break up the questions in many different ways.

Does menthol contribute to the overall risk of developing dependence? Among people that use, does it affect the level of dependence? Among all users, does it have little effect in some populations and a bigger effect on others, or is there a sweet spot effect that was mentioned earlier among people that are earlier in their trajectory of smoking, the six to ten?

I think when we're looking at the dependence-related questions, we have to look at all of those. And by analogy, cocaine gave us a good analogy. Intravenous cocaine was a powerful, effective way of developing a severe cocaine dependence.

Crack cocaine, when that came along, it's not clear that crack cocaine made people more addicted than you could get by intravenous. What it did was contribute greatly to initiation among people that wouldn't have otherwise used intravenous cocaine. So it contributed to prevalence.

I think when we look at menthol, we have to look at the dependence and addiction-related issues from all of these perspectives; does it increase

risk; does it increase the likelihood of initiation, conversion from use to dependence, and so forth.

DR. SAMET: I think we've captured that in the diagrams we've had. But I think it would be useful for you to perhaps put that in writing. And I think, among other things, as we work with David, make sure we have captured these different points of potential impact of menthol as you lay it out because these are aspects of what each of our chapters is addressing. There may be pieces of a model that we would want to explore.

So I think we should make sure we have those with the specificity you just listed them. I think we do, but we should make sure that we do.

Neal, this has caught your attention.

DR. BENOWITZ: Yes. I was just wondering. I think Jack's point's really an interesting one. But did the model look at experimentation? Because that's really an important issue about the transition from experimentation to regular use.

DR. SAMET: So the original figure has experimentation in it. If I recall what David showed

us, there's an initiation without an antecedent experimentation. And I think the question of whether we model those as two separate processes is I think where your question would take us.

DR. BENOWITZ: Yes. I think there's a lot of literature about the importance of the first ten cigarettes. Some people try one or two and stop, and the question is, what happens to the ones who smoke more than two or three? And so I think that's really an important question to follow up on what Jack was talking about.

DR. SAMET: Another box in the model, potentially, particularly if there are relevant data.

Other comments?

[No response.]

DR. SAMET: So let me confer for a moment.

[Pause.]

DR. SAMET: Here's what I'm going to suggest. We're approaching 11:00, when the President has requested that we have our moment of silence. I'm going to suggest that we end our morning meeting when I finish my directions to us here with that minute of

silence.

We're a little bit ahead of schedule, and we would hope that perhaps at 12:30 we could begin our presentation, hoping that our scheduled speaker for 1:00 will be here and available. Just for the committee members, we will be escorted over to the cafeteria for lunch.

So let me make the suggestion, then, that after a minute of silence beginning shortly, that we reconvene at 12:30. So thank you, and let's take a moment.

[Moment of silence.]

DR. SAMET: We'll reconvene at 12:30. Thank you.

(Whereupon, at 11:01 a.m., a luncheon recess was taken.)

A F T E R N O O N S E S S I O N

[12:33 p.m.]

DR. SAMET: Okay. I'm going to reconvene the meeting, and want to welcome everybody back post-lunch.

We're going to move on to hear from Michael Hering, Deputy Chief Counsel for MSA Payments, Tobacco Project, with the National Association of Attorneys General, who will be addressing the issue of contraband and menthol. Thank you for coming to speak with us.

Contraband and Menthol – Michael Hering

MR. HERING: Thank you, Dr. Samet and members of the committee. And thanks to you and for the FDA for inviting me here today to speak to you about the potential effects of a menthol ban.

I'll need to start my presentation with a little bit of a disclaimer. I'm here from the National Association of Attorneys General, an organization whose members are the 50 attorneys general of the United States. I need to let you know that NAAG as an organization has no position

regarding the question of whether menthol should be banned. The views expressed in this presentation here today are not those of NAAG or, in fact, of any of its member attorneys general. I'm really here to speak to you about our experience under the MSA with tobacco products, but not to make any recommendations regarding the potential menthol ban.

Before I begin, I need to tell you just a little bit about who I am and what NAAG is and what the MSA is. Some of you, I realize, may be familiar with this, perhaps very familiar; but for many of you, I expect this is not something that you're generally familiar with.

NAAG, the National Association of Attorneys General again, and specifically the Tobacco Project, which is a division within NAAG with whom I work, or in which I work, assists the states in administering, enforcing, and defending, and improving, where we can, the Master Settlement Agreement. Of course, that begs the question of what is the MSA?

The MSA is a settlement that was entered into a little more than a decade ago at this point, and

the parties to that settlement are the settling states, which are not all the states, but they're nearly all the states, 46 states, D.C., Puerto Rico, and four territories – and, by the way, the four states that aren't part of the settlement have roughly corresponding settlements. And then on the other side, we have nearly 50 tobacco manufacturers, the participating manufacturers, large and small. They include the three big U.S. players, and they include a good number of smaller companies.

Very basically, very basically, I'm going to tell you about the MSA. The MSA covers cigarettes and roll-your-own tobacco, tobacco used to make cigarettes. It doesn't cover, except in limited circumstances, other tobacco products.

Under that settlement, the participating manufacturers make payments to the states in perpetuity. Those payments currently run about $5.60 per carton each year. So for every carton sold in the United States, the participating manufacturers pay the settling states $5.60 per carton. They don't pay on the other products, and you'll see why that's

relevant later in the presentation.

The participating manufacturers are also bound by the marketing and advertising restrictions within the MSA. Now, of course, there's also another class of manufacturers, which is the nonparticipating manufacturers. I don't have a number of those. It ebbs and flows as more come into the market or more leave. But the participating [sic] manufacturers are not bound by the MSA because, of course, they are not parties. They are not bound by the public health restrictions, and they do not make payments. However, they are generally required to deposit monies into escrow, a payment on an annual basis that is roughly the equivalent of, but always a little bit less than, the MSA rate of $5.60 a carton. And that money is held in escrow in the event of a state recovery in a judgment or settlement against that tobacco product manufacturer for health-related claims.

I'd like to talk to you a little bit today about what we've learned by experience under the MSA. The MSA is one of a number of changes, recent

changes, in the regulatory landscape. You've asked me here to talk today about the possible effects of a ban on menthol on contraband. And I'll talk to you about that, but I'd also like to talk to you a little bit about something that I'm calling regulatory or legal evasion.

There have been a good number of changes. Each one of those has resulted in market reactions to those legal and regulatory changes over the years. In many ways, in many instances, it's reacted in such a way as to find a loophole -- the market has found a loophole, a regulatory loophole -- in that regulatory change, which has been exploited to their advantage.

Not all of these evasions are necessarily illegal, but I think it's fair to say that some could be characterized that way. And I'd say, in many instances, even if they aren't illegal, they're certainly something that evade the spirit and purpose of the legal and regulatory change.

I'd note that your -- or I should say the FDA's mission or stated purpose in Section 907 is to determine whether the use of menthol in cigarettes

should be restricted. Cigarettes is the only product mentioned. I don't see the other tobacco products mentioned in Section 907.

My understanding is, also, that FDA -- at least not yet to this date -- has not asserted jurisdiction over other tobacco products such as cigars, which you'll see becomes relevant later in the presentation. However, I do know that they issued a preliminary notice of rulemaking on that subject.

Looking down this list, there have been a number of changes, as I said. I've listed, of course, the advent of the MSA first. Together with the MSA, we have escrow statutes that go along with the MSA. Those are the ones requiring the NPMs to deposit monies into escrow. We have state directories of certified tobacco product manufacturers. These are state laws under which a tobacco product manufacturer must certify before it can sell legally in those states.

We have federal and state tax increases and extensions of the tax, meaning that in some instances

the feds, and in some instances the states, have extended their tobacco tax to a product that had not previously been taxed. The most notable among those is the SCHIP bill, the State Child Health Improvement Program bill, which was passed in April of 2009, I believe.

We have federal assessments, not taxes, necessarily, but other assessments against the sales of the tobacco products: the farmers' buyout that collects money under USDA to pay the farmers for their growing quotas; an assessment under the FDA Act. We have, of course, state and local tax increases, which have been numerous over the years. We have changes in federal law and regulation such as the Gray Market Ban, which prohibited, shortly after the MSA, the reimportation of product made by major manufacturers, domestic manufacturers, and intended for foreign sale. We have the Imported Cigarette Compliance Act, also directed at imported cigarettes. We have the Coble Amendment and the PACT Act directed in large measure at internet sales of cigarettes. And, of course, we have the FDA.

We also have state examples of legal and regulatory changes. There are many of them. I've just simply listed one, which is the reduced ignition propensity, or the fire safe compliance laws, that have been enacted, I think, in a number of states. I don't have a number for you, but I think at this point it may be the majority.

As I said earlier, each of these has resulted in some sort of market reaction. In many instances, the industry has moved in some way to, as I say, evade, sometimes in a legal fashion, sometimes in a questionable fashion, but nearly always in a way to evade the spirit and purpose of those laws.

I'm going to give you two examples, or I'm going to delve a little bit more deeply into two examples. The first one is the example of little cigars.

This first came to our attention when we had, in the wake of an enforcement action against an MSA-participating manufacturer -- without going into the details, I'll just tell you that this enforcement action resulted ultimately in a consent judgment

whereby the principals of that tobacco product manufacturer agreed to essentially stay out of the cigarette business for a period of five years. In fact, that was part of the court-mandated settlement or judgment that ended that suit.

Lo and behold, shortly thereafter, I discovered that the principals, while they had been banned from the cigarette business, started right back up in the little cigar business, which we had not, I suppose, had the foresight at the time to include in the consent judgment. And I've put together a slide showing you only some of the differences between cigarettes and little cigars. There are actually more than this.

But on the left, the Marlboro up here on the screen is, of course, a cigarette. On the right, the Winchester is a little cigar. I've listed one, two, three, four different characteristics and explained the differences.

The MSA escrow statutes, or the MSA or escrow statutes, depending -- the MSA would apply if you are a participating manufacturer; the escrow statutes

would apply if you're a non-participating manufacturer. In either case, if you make a cigarette, you either have to pay the MSA rate of about $5.60 a carton on that cigarette, or if you are a nonparticipating manufacturer, deposit the equivalent amount into escrow. If you're, again, making a cigarette, you're covered under that. If you are making a little cigar, you're not covered because the MSA, of course, only applies to cigarettes and RYO, not to cigars.

There are state statutes that require entities to certify and be placed on a directory before they can sell in a state. Likewise, those statutes cover cigarettes. They do not cover little cigars or cigars at all.

The federal excise tax rate -- and this is pre-SCHIP, pre the increase in SCHIP -- was $3.90 per carton; the comparable rate for little cigars, 37 cents a carton. State excise tax, of course, this varies by state. But the average -- and this is the current average, actually; I wasn't able to obtain a historical average. But the current average is

$14.50 per carton.

The average for little cigars is not available, but I can tell you that it's usually not even an excise tax rate. It's usually an OTP rate, other tobacco rate, which are typically an ad valorem rate. In other words, rather than pay a unit based per cigarette or per pack or per carton, it's a percentage of the wholesale price, 20 percent of the wholesale price, 15 percent of the wholesale price, 50 percent of the wholesale price, which is often less for these products than for cigarettes.

All in all, if you do the math, we're talking about an advantage of somewhere around the order of $20 a carton financially between the product on the left and the product on the right. But, of course, it's not just the financial aspect that we're talking about here. There's also the ability -- we saw this, in fact, with manufacturers that had -- who for reasons that I won't go into were not able to certify their cigarettes in a state to be able to sell cigarettes in a state.

They could, and did in some instances, begin

selling little cigars, which of course did not need to be covered under the state directories, and therefore they were able to sell where they otherwise would not be able to sell had they been selling cigarettes. So it's not just necessarily a financial evasion; it's also a regulatory evasion.

I should mention, I think, before moving on -- I don't have a slide on this, but the brand Winchester, there's a history to that brand. This legal and regulatory evasion goes all the way back to the Federal Cigarette Labeling and Advertising Act, FCLAA. There's a paper out there you might be interested in taking a look at that examines the market reaction in the late '60s and early '70s to FCLAA. And, essentially, the birth of little cigars of this type go back to FCLAA, where Congress, initially, at least, extended FCLAA only to cigarettes and not to cigars. The industry at that time saw an advantage in creating a cigarette-like cigar that could be advertised and marketed in ways that were banned under FCLAA.

Congress did eventually extend FCLAA to

include cigars. But I think what the industry learned during that time period was that there were significant advantages to calling their product a little cigar. And it wasn't necessarily just the ability to market in ways that were foreclosed to cigarettes; it was also a financial advantage because even after FCLAA, the rates on the products were not equalized.

Let me now talk about what happened post-SCHIP. Again, SCHIP is the State Child Health Improvement Program, and it significantly changed the federal excise tax levels for a number of tobacco products, including cigarettes and little cigars. Cigarettes went from $3.90 a carton to $10.07 a carton. And because, in part, of the advocacy of a number of public health groups and others, Congress did decide to equalize at least the federal excise tax rate between cigarettes and little cigars. So little cigars are currently also at $10.07 per carton.

Now, that didn't necessarily mean that the rates were equalized at the state tax level. State

excise tax rates are still -- there's a differential between cigarettes and little cigars. But the more interesting aspect is what happened over here with large cigars.

Now I have to explain what I mean by large cigars because I think many of you, when I say large cigar, are thinking about the kind of thing that you would have seen dangling from the -- maybe not the lip, but the hand of Castro or Churchill, you know, the big stogie type cigar that are often made in Cuba and come in a mahogany box.

We're not talking about those. We're talking about -- when we say large cigars, that's a tax classification. And that simply means cigars weighing more than 3 pounds per thousand. And I can tell you, I actually picked these brands that are bookmarking Winchester deliberately because I can tell you -- I will represent to you that these brands are made by the same manufacturer in the same North Carolina factory.

I don't have them here, but you can see from the picture that the package is the same size. The

diameter of the tube is the same size, same length. The filter appears to be about the same length. Yet this is classed as a cigarette, meaning -- and by definition, a cigarette weighs less than 3 pounds per thousand because otherwise it's a large cigarette, of which there are none on the market.

So this weighs less than 3 pounds per thousand. This identical package, same factory, probably coming off of a line right next to the line that this was built on, is a cigar, not a small cigar but a large cigar, one weighing more than 3 pounds per thousand. Now, I haven't weighed them. I'd guess that it's 3.01 per thousand. But the reason that this was done was quite deliberate because you went from a federal rate of $10.07 per carton to 50.75 percent of the wholesale price. And I will tell you that that is generally around a tenth of what this might be, much, much less. And, again, you're able to not be covered by the MSA or the escrow statutes, the state directories. You're at a lower federal rate. And again, you're at a lower state rate versus the cigarette.

Next example with cigars, or the next step in the cigar evolution, and this is post-FDA. One of the things that FDA has done, of course, one of the first things that went into effect, was the flavoring ban. But, again, the flavoring ban at this point only covers cigarettes. FDA has not extended it at this point to cigars, either large or small. I realize that may be coming down the road, but I'm talking about the present tense.

So what can we expect from the market reaction there? The products -- I'm going to back up a little bit so I can point. The products on the left and the right are both made by the same company. This is actually an MSA-participating manufacturer. These are clove products. The product on the left, in this instance -- I'll start with the product on the right.

These are clove cigarettes, post-FDA, and this is the package over here, clove cigarettes, made by Djarum, made in Indonesia. They're not the only ones, of course, in the market, but this is one of the leaders. Shortly after the FDA ban, these

arrived in the marketplace, clove cigars. You can see, of course, the difference between them, not very much.

Likewise, we have other flavored cigar products. It's hard to read, I realize, but these are large cigars here. I'm not sure whether these are large or small. But I'll tell you, and I realize you may not be able to read the flavors, but on the left here we have cherry, peach, strawberry, and grape. Over here, for the happy hour cocktail-flavored cigars, we have piña colada and appletini, I think, which are only two of the cocktail-flavored varieties.

Again, a regulatory way -- or an industry reaction evading a regulatory change; certainly, again, if not evading it in the legal sense, evading, of course, I think the spirit and purpose of the FDA flavoring ban on cigarettes.

That's it for little cigars, or large cigars, for that matter. One more example I'm going to give you is RYO versus pipe. Again, we have two products here that were very similar in a similar way to which

cigars and cigarettes were similar. We have RYO and pipe. Under the MSA, again, RYO is covered; pipe is not covered. State directories, again, RYO is covered; pipe is not covered. Federal excise tax rate is pre-SCHIP, the same per pound, 1.0969; state excise tax rate usually the same, usually, again, an OTP rate at an ad valorem rate, not a unit-based tax.

Post-SCHIP, I've highlighted the two changes in red. What happened was Congress decided to equalize, essentially, the tax rate for RYO with cigarettes. The rate of $24.78 per pound is essentially equal to the $10.07 per pack -- I'm sorry, per carton, assuming a conversion rate of, I believe, .0325 ounces per stick, whereas pipe went up by nowhere near as much. We now have pipe that is very roughly one-tenth -- taxed at the federal rate at one-tenth the amount of RYO.

So you're looking at a huge difference here. And don't forget that this represents another $5.60 or so a carton. So when you add the $24 and the $5.60 a carton, you're nearly in the high 20s in terms of dollar differential. Again, you've also got

very significant regulatory differences.

What was the reaction of the market? For those that can't see it, the red line that goes from down here to up here, this is pipe volume from January of '09 to the latest data that we have for September of 2010. Green line, RYO volume.

Where is this pipe going? One thing I'd like to -- for those of you that haven't seen these, there are out in the marketplace now a growing trend, RYO vending machines. These are machines that have appeared in convenience stores and smoke shops around the country.

The way it works is there's a little hopper at the top of the machine, right there. You take your tobacco, you pour it into the top, into the hopper. You take your empty tubes. You slide them into a tray. I think it's -- the tray might be there or there; I'm not sure. And what pops out in about eight minutes per carton, a carton full of cigarettes.

Now, if you're pouring tobacco in the top here at a rate of $24.78 per pound, you're not really

generating any tax savings. But, of course, if you read this quote, you'll note that the real benefit is billed as a cost savings. And if you go on the website, there's a lot more about this, the RYOfillingstation.com website.

But, essentially, what they're expecting people to do and what in fact does happen is no one goes up there and fills that hopper, as far as I can tell, with RYO tobacco. What they're filling that hopper up with is the pipe. Again, an evasion, at least -- if not a legal evasion, an evasion of the spirit and purpose of the law.

I'll let you know, just as an aside, that TTB made an effort to essentially change the status of these machines to require licenses for them, and that effort has been stymied by the entry of a preliminary injunction in a lawsuit brought by the manufacturer and users of these machines.

What do I expect in terms of -- I'm trying to draw an analogy here, of course, to the menthol. What could I expect were FDA to put into effect a ban on menthol cigarettes and to not cover other classes

of products? Well, you can probably guess from my presentation, the first thing I'd expect to see -- and by the way, all these pictures and all these products are already on the marketplace. It's not that I expect them to be created because they already exist. It's simply that I would expect them, of course, to grow in popularity and in sales.

So the first thing I'd expect to see is menthol cigars. And I've said cigars. Some of these are little cigars, and some of these are -- the ones on either end actually are little, meaning they weigh less than 3 pounds per thousand. The two in the middle are large.

But menthol cigars. These are menthol cigars with filters. They are generally the same diameter and length of cigarettes. They have filtered light cigarettes. Essentially, another way I sometimes call these are brown cigarettes because to the naked eye, the only distinction between these and a cigarette is simply the fact that they're wrapped in what appears to be brown paper. And the paper contains some level of reconstituted tobacco, but not

enough that -- it certainly isn't a natural leaf.

What else? Menthol RYO. And, again, this is already out in the marketplace. But, of course, given the tax differential between RYO and pipe, what I'd really expect to see is an uptick in menthol pipe tobacco, which again is already on the market.

If you can't get menthol pipe tobacco or menthol RYO, you can get menthol tubes and rolling papers to stick in those machines that you've seen. And, of course, if that's not available, there are menthol filter tips to add the menthol flavoring.

Last but not least, I would expect there to be after-market mentholation of the products. I had the opportunity to visit a cigarette factory; it was actually the Philip Morris factory in Richmond, I think one of the biggest factories around. And I learned -- at least, this was not known to me; it may be to some of you -- that the cigarettes coming off the line are not mentholated when they come off the line. What happens is there's foil that wraps the cigarettes before it goes into the cardboard. The foil is coated with menthol.

The product is then wrapped in this foil. It looks like aluminum foil. I don't know whether it's -- it's metallicized in some way. I don't know what the characteristics are. And then the product, of course, absorbs the menthol over time.

I would not imagine it to be too hard for people to start marketing boxes that you stick your cigarettes in, throw in a tablet or two, throw in a few drops of menthol, mentholate your own cigarettes. And, in fact, it's not too hard, if you Google around, to find drops of menthol flavoring already available.

I would expect that to increase, perhaps, as I say, with a fancier sort of kit with a box or tablets or the little capsules that you break. You might even see the sorts of filters -- if this was an infringement, of course, on the RJR patent, I imagine they have filters with the little capsule like the Camel Crush has to add the menthol at that stage.

So before I go on, let me just say that I've been talking to you thus far about essentially what I've termed evasion. But you did ask me to talk

about contraband, and so I do have just a couple slides on the contraband, direct contraband, rather than evasion.

I think there'd be some differences between contraband under a menthol ban and the contraband we have now. The thing about the contraband we have now is that you can't necessarily pick up a pack of cigarettes and determine whether it is contraband or not because when we talk about contraband, we're talking about a whole host of things.

We're talking about the evasion of federal taxes. We're talking about the evasion of state taxes. We're talking about counterfeit product. We're talking about product, in my world, at least, that may be sold in a state where it is not on the state directory. It's not a certified product. We're talking about a product sold in a fire-safe state that is not fire-safe. So all of those would be classes of contraband.

Again, if I were to pick up or hold up a pack of cigarettes and hand it around, none of you would be able to determine whether it was legitimate or

contraband because looking at a package, it's very hard. Essentially, you have no way of knowing whether federal taxes have been paid.

If you're in a state with no stamp, you also have no way of telling whether state taxes have been paid. If it has a stamp, at least there's some indication, but of course that stamp could be counterfeit. The pack could be counterfeit. And then you don't know whether it's fire-safe. Well, you could look it up on the directory and determine whether it's on the directory, and it may be listed as fire-safe, but without actually testing it, you're not sure.

With menthol, I think a lot of those problems go away because menthol would be, of course, per se illegal. You spot a menthol pack on the street, on the shelf, anywhere in the chain of distribution, and you would know it's illegal. So a lot of the problems that we face in law enforcement as going after menthol as regulators and law enforcers, going after contraband currently would not apply to a menthol ban, again, because it would be essentially

per se illegal.

So it would be easier essentially to identify, I think. But it wouldn't be a perfect world because there are some opportunities out there. Currently, as far as I know, there's no federal reporting and very limited state reporting by cigarette brand or style. So were you to try to determine what's going on in terms of importation of cigarettes and look at the records that way, that simply doesn't crop up because it's not a categorization under the Harmonized Tariff Schedule, which is the schedule that Customs uses for imported cigarettes.

Likewise, it doesn't appear on any of the federal taxing forms. It generally doesn't appear on the state taxing forms. The states do keep track of brands for other reasons under the MSA, but oftentimes those don't include the style.

Then, of course, there's always the potential -- I wouldn't expect all the smugglers, at least, to identify their product on the label, certainly not on the outer label, as menthol.

Certainly, I would imagine the outer carton is not going to say it's menthol; they are at the case level. The carton level probably won't say it. They might put it on the pack because of course they have to advertise it. But there's also the possibility that they simply put some sort of secret code on the product, I suppose, to let people know, in the know, that this is menthol. Of course, I imagine you'd be able to smell it if you couldn't do anything else.

What are the likely sources of contraband? Where is it going to come from if we have a ban on menthol in this country? Well, of course, as far as I know, menthol isn't banned in any other country. We've got Canada on the north, Mexico on the south, and cigarettes coming from everywhere else as well, all around the world. We've also got some unlicensed domestic manufacturers, primarily located on Native American reservations currently. But there are some -- I've heard from ATF anywhere between a dozen, 15, maybe even 20 different unlicensed manufacturing facilities in the United States.

I expect we'll also have domestic companies

manufacturing menthol, not for sale in this country but for sale in other countries. The opportunity, of course, would exist to divert that domestically-made product back into the U.S. market. That is currently one of the contraband schemes that goes on as a tax dodge. In other words, product that is made here in the U.S. will be shipped offshore and then secretly re-imported, or in some instances there are simply empty containers that are shipped off or containers filled with cardboard or scrap to make sure they weigh the right amount, whereas the actual product, the cigarettes, stay here in this country.

I imagine there'd also be off-the-books manufacturing by domestic manufacturers, something that happens -- you know, they have four shifts they report about, and then they have that midnight shift they don't tell the Feds about.

Then there's the aftermarket manufacturing. I term it manufacturing. And I don't know whether that would happen -- and by that I mean -- let me just be clear again what I'm talking about. I imagine what I said earlier could happen perhaps on a

semi-industrial scale, that some enterprising soul out there might decide to buy a whole bunch of Marlboros or Camels or what have you that are unmentholated and then open up the packages, pull them out, run them through a process that mentholates them, and then put them right back in and sell them. I think that's certainly a possibility.

Likely methods of distribution: Well, I mentioned that PACT and Coble had been passed and are trying to take a bite out of the internet sales, which are of course a form of delivery sales. By that, I mean sales usually delivered by mail or courier or others.

Right now, there's a limited ability to stop international mail from coming into this country simply because Customs and the Postal Service have their hands full, of course, with other dangerous products. I don't mean to say that they aren't trying; they are. But some of it makes its way through.

Likewise, there is still the ability, we've learned, for some persons to evade the ban under PACT

on delivering cigarettes in the mail, and that's done sometimes by simply not declaring them as cigarettes, although I think you can only do that on a relatively limited scale. Other instances, it's done by trucking them and using local couriers.

There is a Native American distribution network, a growing Native American distribution network in the country. Of course, Native Americans are subject -- while I represent, generally speaking, states, Native Americans are co-equal sovereigns to the states. However, of course, they are subject to federal law, and presumably they can and would generally abide by the federal law, and the federal government would have the ability to control them to some degree. But I do wish to at least let you know that this distribution network does exist.

We have at least one tribe that has declared that they have the ability, because of their treaty rights, to travel freely throughout the 50 United States and to trade. And by that, they mean at least at the state level and to some degree the federal level because they claim essentially immunity to, I

believe, in part, PACT, which is a federal law as well, that they do not need to abide by the general requirements when they travel and trade; in other words, that they can freely distribute cigarettes from one tribal area to another tribal area throughout the country.

I don't know where that will go. We're still dealing with that in the courts. But certainly the potential exists for an alternative distribution network in that mean.

Then there's what I just call the white van network. And this, of course, is the purely illegal cigarettes, someone driving to a manufacturer that's made them off the books, or perhaps to a reservation, or to a bad wholesaler, filling up the white van, and bringing them to the bodegas in the Bronx or other major cities.

I've gotten a picture here of what the Feds are seeing in Canada. I haven't heard a lot about these showing up here in the U.S., but these are what are known as "rollies." These are cigarettes simply manufactured, put into a Ziploc bag. Sometimes they

throw in -- you can see; it's hard to see, but this is a kind of surgeon general's warning. I don't know why they put that in there other than perhaps some veneer of legitimacy. And then these are distributed. In fact, in Canada I've seen quite large estimates for how many of these are being distributed up there. They haven't shown up in large numbers here in the U.S., but I did want to let you know about them.

Now, one thing -- let's see. I think that is the end of my presentation. One thing I did want to tell you is I've identified, I think, some of, as I say, the regulatory problems. I've identified where these cigarettes might come from. I've identified how they might be distributed.

What I haven't done, and I don't think I can do, to be honest, is to give you necessarily any kind of hard estimate about the volume, what I may or may not expect. Certainly I don't believe it's going to be zero. I don't believe it's going to take over the market; somewhere in between. But I have not attempted and really could not give you any more than

very much of a guess about the sort of volume that we might be talking about. But in making this presentation, I hope to give you an idea about what at least I would expect in terms of a market reaction to a menthol ban and where you might see the problems.

So, with that, I'm done, and available for any questions you have.

DR. SAMET: Thank you very much for your presentation.

Let me open up for questions. And to the committee, we actually have up till the time of the open public hearing for discussion, or we may choose to discuss this presentation specifically, go on to the open public hearing, which covers some of the same topic, and then come back and discuss further.

But let me open now for discussion. Jack?

DR. HENNINGFIELD: Just a question about capacity. I don't remember the numbers of how many billion menthol cigarettes are presently sold in the United States and required to maintain the current level of menthol smoking, but I know it's many

billions.

What is the capacity? What is your sense of the capacity? And the reason this is relevant is oftentimes, contraband is put up as an all or nothing. You know, if you ban menthol, then there's going to be contraband. But I think the assumption is that whatever you do, there's always going to be some contraband. The public health impact is related to capacity.

So do you have any sense for the capacity of any of these systems to rival the current distribution networks in convenience stores? And again, by way of example, what we found in Canada was that when there was -- it wasn't just smuggling through suitcases. It was large. You know, it was trucks. That's what it took to make a dent.

Your sense of the capacity?

MR. HERING: Well, let me thank you for the question. It's a good question, and it touches upon the area where I'm less of an expert, but I will attempt to answer it.

Let me say first of all that in regards to --

when you're talking about capacity, I'll go back to the first part of my presentation again, what I've termed the regulatory evasion. Conceivably, there's no limit to the capacity of a factory to swap their machines over to making menthol cigars because they are made on the same equipment with the same raw materials. The only difference is presumably changing the mix a little bit of the blend and changing the kind of paper you're using, from paper to paper containing some level of reconstituted tobacco.

So if that is a viable alternative for menthol cigarette smokers, I'm not sure there's any limit to the capacity; likewise, for some of the other alternative products.

However, if we turn your question to the pure contraband, not the alternative products but to the contraband, it's not so much, again, I think a capacity for manufacturing because menthol cigarettes would be freely available in Canada, in Europe, South America, all around the world. It's really a limit of how will you can distribute them, I think.

That is hard to judge because it depends, of course, on the federal and state reaction in terms of their ability and resources and commitment to enforcement. I think in Canada, in part what you're seeing, to be perfectly frank, is an unwillingness to enforce in certain ways and against certain persons that has allowed that market to flourish. And I don't know that we could necessarily draw a parallel from the U.S. to Canada without knowing our reaction to those sorts of questions. I think Canada is different in that respect.

So, again, I think it would be limited to your methods of distribution. And looking at -- oops, went to power save -- well, I was going to refer to my slide again, but -- oh, thank you. I'll go to the last slide. All right.

Well, looking at the methods of distribution, there's only so much you can do with some of those methods of distribution. You can't have menthol cigarettes advertised as such on the shelf, I believe. Unless law enforcement totally abdicates its responsibility, presumably people are going to

seize those. They're going to see them. They're going to take them away. Then, again, you can't cover every shop in the United States, and there's going to be some down behind the counter, in the back room, for the people that know how to ask, at least in certain shops.

So my gut feeling is that you could not replace the demand that you have today. It would be less, but of course you'd always have a contraband problem, which I think you've acknowledged you always do.

DR. SAMET: Tim?

DR. MCAFEE: Well, thank you very much for a very interesting and very disturbing set of information. I have two questions. I'm going to ask one now. It's essentially whether we could look more at the experience from banning flavored cigarettes and draw any potential analogies with the likely experiences around both contraband and also the attempts by the industry to shift people to cigars.

So I'm curious if you know. And if you don't, I perhaps am suggesting that this is something

we should try to look into, is how successful these efforts have been at replacing the cigarette market for, for instance, cloves with cigars, where we know we have them. And do we know whether there have been instances of any of the types of contraband or other ways at the individual level to get around this?

MR. HERING: Thank you. I think, specifically with cloves, there may -- and I do not have this data, but I do think it might be available, or more available than some of the other categories, for you to examine simply because clove cigarettes are largely imported, and when they are imported, they are a separate HTS code, Harmonized Tariff Schedule code. So we do have historical statistics on how many clove cigarettes have been imported over the years.

Presumably we also have -- well, I take that back. I don't know whether we have an equivalent code for cigars, for clove cigars, whether you'd be able to determine whether there's been a one-for-one shift between the disappearance of the clove cigarettes and the advent of the clove cigars. But

that would be an interesting thing to look at.

When it comes to the flavoring, I don't know that we have any records on the volume of flavored cigarettes because, again, there are no real records that I'm aware of at the federal level or, for that matter, at the state level that would keep annual/monthly volume reports on flavored cigarettes, and now flavored cigars.

I have actually attempted to break down some of the TTB data, TTB being the federal taxing agency, when it comes to the cigars, my interest being in what -- as I mentioned to you, there's a small cigar category and a large cigar category. What I was trying to determine was how much of the large cigar category -- the really big ones, the ones that we really think of as being cigars -- versus how many are these ones that are, say, over 3 pounds but less than 4 pounds, or certainly less than 5 pounds per thousand, you know, the ones that are very cigarette-like.

Unfortunately, without going through manufacturer by manufacturer, which I am not able to

do because I do not have access to those records; it's not something that can be determined. But I do agree with you that it would be an interesting question.

DR. MCAFEE: Great. And there isn't anything on contraband that you -- contraband --

MR. HERING: The volume of contraband?

DR. MCAFEE: Yes.

MR. HERING: There are a number of estimates out there on just the overall levels of contraband. The GAO is working on one as we speak. They've done some in the past. There have been some congressional reports.

Of course, the very nature of contraband is that if it's done right, you don't know about it, and it's a hard thing to estimate. It necessarily has to be done by projection, you know, taking a small amount and then giving it your best guesstimate as to how much of a market that represents, the part you know about.

DR. MCAFEE: And even if that were accurate for contraband in general, we'd be even less likely

to have an estimate around what's been happening around, for instance, flavoring, like cloves.

MR. HERING: Clove or flavored contraband?

DR. MCAFEE: Flavored contraband, yes.

MR. HERING: I suppose not. But, again, I think that to the extent -- at least in anecdotal evidence, and this is anecdotal evidence alone, I have seen websites where these products are available, internationally available for sale online. So that would depend upon delivery by international mail.

You can still order clove cigarettes from abroad. Whether they can actually get here or not depends upon, of course, how well we're able to stop them as they come in, likewise with the flavoring; although what I don't know is whether people necessarily will bother with doing that when they have the alternative of buying a clove cigar or an appletini or cherry-flavored cigar rather than the cherry-flavored cigarette they might have smoked before.

DR. MCAFEE: Thanks.

DR. SAMET: Mark?

DR. CLANTON: In my experience over the last ten years or so testifying before state hearings about taxes and tobacco, the question always arises about contraband, and I guess diversion is not the right term, but contraband as it relates to loss of tax revenue. That question that seems to come up every time about taxes and tobacco leads me to believe that when states do enforce laws related to contraband, they do so to protect tax revenue.

So I'm going to ask you to speculate, if you care to speculate. Do you think that, in the menthol case, in the scenario of a menthol ban, would states have a lesser interest in enforcing a ban as it would not relate to tax revenue anyway?

MR. HERING: My own opinion is no. I do not think states would have a lesser ban. I do not believe that they enforce purely for revenue purposes. Of course, that is a major aspect or motivation. But I believe that, at least in my experience and with the people that I work directly with -- and I do work directly with somebody in every

state, oftentimes the tax people, the public health advocates and the AGs. The motivation goes beyond tax. I would not characterize that.

I'd also point out that -- well, you've asked about the motivation. It's a very different situation when you're talking about -- a lot of the tax revenue losses that they're talking about again have to do with a different kind of evasion than we're talking about here, the arbitrage between a high tax and a low tax state, moving it from North Carolina to New York, counterfeit stamps, things like that.

Menthol, as I tried to say a couple slides ago, would be an entirely -- it's apples and oranges when it comes to the contraband, I think, because we've never really had -- the close example might be the flavoring ban, not one of these types of contraband where you're evading FET or you're evading SET.

But I certainly would believe, to go back to your question, that folks in the field would be just as ready to enforce against an illegal contraband

cigarette as they would against a cigarette where the tax has not been paid.

DR. SAMET: Jack?

DR. HENNINGFIELD: On this capacity issue, I'm not sure how relevant it will be for TPSAC report deliberations. But I think the FDA will need a more extensive evaluation of capacity to provide menthol cigarettes under a ban of legitimate menthol cigarettes under various scenarios of control; because with all addictive drugs, the risk of addiction and prevalence of addiction and use is related to supply and cost, whether the species is rat, monkey, or human, whether the drug is cocaine, heroin, or nicotine.

So there are some scenarios under which if capacity to provide illicit menthol cigarettes is as free as it is today, you know, to readily supply the needs of 15 to 20 million Americans, well, then a ban would not provide a public health benefit. If, on the other hand, the capacity is much more limited, then it may be possible for some people to meet their needs and others to try them. But a ban could still

have a tremendous public health effect in principle.

But I think the FDA really needs an examination of the capacity issue because you've showed us several different routes of manufacture, several different potential routes of distribution, and this is very illuminating. Now what I think we need are some models for what could happen under different scenarios.

DR. SAMET: Tim?

DR. MCAFEE: My second question essentially boils down to whether you have any insights into what it would take and what the likelihood is of doing what seems sort of patently obvious around this one, the prime evasion tactic of creating essentially cigars that are really cigarettes, and why all the various parties that could potentially alter this have been so slow on the uptake to close this loophole, and what you think the chances are of it being closed in the current scenarios and then also in the scenario if menthol were to be banned.

I realize there would probably be other creative solutions to it, but what do you think could

be done about this particular one?

MR. HERING: That's a good question, and there are a number of possibilities. The easiest and clearest would be for these products to be -- and I would represent to you that I think a number of them are more properly characterized as cigarettes than as cigars under the current federal definition.

The problem is -- and I don't know how many of you are familiar with the federal definition. The problem is that the federal definition is a subjective definition. These are cigarettes if people think they are cigarettes, if people are likely to buy them as cigarettes.

I look at them. Some of the data that I look at suggests that people do think of them as cigarettes, are likely to buy them as cigarettes, and therefore they are cigarettes, in which case, of course, the flavoring ban applies, and if there's a menthol ban, the menthol ban would apply.

FDA has the ability to offer regulatory guidance on its federal definition of whether these are in fact cigars or cigarettes. That is something

that could occur. Likewise, TTB, which has overlapping jurisdiction from a tax standpoint, has the ability to offer regulatory guidance on whether these products are cigarettes or are cigars. In fact, TTB took the initial steps of promulgating proposed regulations that have been out there for some years. They've never been finalized.

Obviously, Congress also has the ability to clarify or modify the definition. Those are some things that could be done. Alternatively, of course, if you decide that these are not cigarettes -- because that's one possibility, is to say, well, these are actually cigarettes, in which case the ban applies -- alternatively, you extend the ban to these products. You assert jurisdiction over the cigars, and you also ban these products.

Again, I'm not here to advocate any position on that. I'm simply here to try to educate you on the broader scope of the issue and to suggest that -- and, again, without taking the position on whether you should or should not, were you to do it, I suppose what I am suggesting is you ought to consider

how the ban would affect these other products, and would it be appropriate to and could you extend it to these companion products so that the ban would be effective.

DR. SAMET: Arnold?

MR. HAMM: Thank you. This kind of goes to Jack's question, and it's also a question to Michael. It goes back to the self-mentholation kits and talking in terms of capacity. And you may not be the person to answer this, but does FDA have the jurisdiction to regulate menthol by itself, just in terms of the self-mentholation kit? Because that could have everything to do with capacity instead of little cigars or what have you.

MR. HERING: Yes. You know what, I -- I'll hold that, let somebody else go first.

DR. HUSTEN: I was just going to say that the definition of a tobacco product does include components, parts, and accessories.

DR. SAMET: Michael?

MR. HERING: And I was going to suggest that -- and, again, I was trying to draw an analogy.

I don't know the answer to your specific question, whether FDA has the jurisdiction. Other people would know better. But when you come to capacity, of course, people have been able to roll their cigarettes, their own cigarettes, and do, and have been doing it for eons, I suppose, or at least as long as tobacco's been around.

But when you talk about capacity, that is where a machine like the one on this slide comes into play because there's a difference, of course, between taking out your paper, pouring your tobacco in, licking it, and rolling it, and getting one of the little home kits that you can make two or five cigarettes at the time in one of these.

Most people aren't going to be able to buy one of these and put them in their garage, not unless they're selling to their friends and neighbors. And then that raises the issue of the legality of this, of when you talk about self-mentholation, whether it's something that FDA can control whether individuals do it, versus whether FDA can control whether it can be done at an industrial leave.

Certainly, they would have jurisdiction, I think, over a company, a manufacturer, doing it. That's what they do have jurisdiction over. When you get into the grey area where I think we would say you do have jurisdiction, but there is some question currently, is over these sorts of machines.

So I was trying to suggest you have to ask the question, when you're talking about capacity, as to the method of making these as well. You can only do so much at home. When you talk about getting enough capacity to fulfill the demand that you're talking about, you need to talk about a large scale.

DR. SAMET: A question. Some of the materials we've been provided that we'll hear about later discuss the criminal aspects of what could happen around contraband and trend. Do you have any lessons learned from experience to date around some of the tactics you discussed around the MSA, the market reactions, the various contraband movement, and so on; who's doing it, how much is involved, law enforcement costs, other aspects of the problem?

MR. HERING: Yes and no. I do have some. I

think I've tried to draw you to the -- I think my presentation has focused on the most, I think, relevant lessons learned. I'm trying to think of anything to add.

The thing is that much of our experience is with a very different type of evasion. It is an evasion by selling cigarettes that aren't on our directories, by moving cigarettes from a low tax state to a high tax state, from counterfeit cigarettes, cigarettes that have been exported and then reimported. But almost all those are not the sort of thing that would directly -- that would analogize to the menthol ban because, of course, you're not playing those games, I think, when you're talking about menthol because you're not trying to evade a tax or a state ban. You're trying to evade a federal ban.

So I think of those, there are only a few that would be utilized in a menthol ban. One of them is the export and then reimport. I would expect that scheme to be used. It is used currently. Certainly it could be used in the future because, again, I

presume that you're not going to ban -- I'm not even sure you have the jurisdiction to ban; I haven't looked into it -- the manufacture domestically of menthol cigarettes for foreign markets. If that isn't banned, then those cigarettes will be made here for foreign markets, and there'll be the opportunity to divert them on their way out of the country, or indeed to reimport them once they've gone to Panama or to South America or to some nearby port.

DR. SAMET: And in terms of current counterfeit cigarettes sold, do you have any sense how much of those cigarettes are made outside of the U.S. and brought in, as opposed to other routes?

MR. HERING: To be honest, the industry would be a much better source for information on counterfeit cigarettes.

DR. SAMET: Dorothy?

DR. HATSUKAMI: I was wondering, is it legal to have brand name extension to cigars? So can you manufacture a Newport cigar, for example?

MR. HERING: Speaking off the top of my head, I'm not aware of anything that would prevent that

from being done. I'd have to think a little bit longer before giving you a more definitive answer. But I can tell you that -- let's see, I just happen to have the example of one of them.

This brand, the Cheyenne brand, which is here, they make RYO. They make cigarettes. They make little cigars. It's all Cheyenne, just as an example. I suppose I cannot think of any reason there couldn't be a Newport little cigar or cigar over 3 pounds per thousand, which is probably what would be done.

DR. SAMET: Other questions for Michael?

[No response.]

DR. SAMET: Good. Thank you very much for your presentation.

MR. HERING: Thank you.

DR. SAMET: Now, we have on our agenda, actually, committee discussion of this issue, which we've not discussed yet. We also have the open public hearing to come, where some of the same territory will be covered.

So, actually, what I would ask the committee

is whether you would want to go on to the open public hearing. I need to check and see if our speakers are here or whether we want to have additional discussion now on this topic.

Preference? Public hearing.

And let me ask -- at least the note I have, speakers 1, 3, and 8 –

[Pause]

DR. SAMET: Anyone who's registered who has not signed in, if you could do so, I think that will let us know that you are here.

So I think what we'll do is we will take roughly a ten-minute break while we sort this out. And, again, if you've signed up for this public hearing and you have not signed in, please do so. We'll reconvene in ten minutes.

(Whereupon, a recess was taken.)

Open Public Hearing

DR. SAMET: Okay. Just before I read the statement introducing the open public hearing, I recognize that we have moved the time. And at least as of now, speakers 1, 6, and 8 -- this is George

Della, Dave Bryans, and Jitender Sidh -- have not signed in. When they arrive, or if they're here, please do sign in, and otherwise we will move them to the end of the hearing. So the first presenter will be those signed in as number 2, Carlton and Flyer.

Before we begin, I'm going to read this statement with regard to the open public hearing. Both the Food and Drug Administration, the FDA, and the public believe in a transparent process for information-gathering and decision-making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement, to advise the committee of any financial relationship that you may have with a sponsor, its product, and if known, its direct competitors. For example, this financial information may include the sponsor's payment of your travel, lodging, or other expenses in connection with your

attendance at the meeting.

Likewise, FDA encourages you at the beginning of your statement to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this committee place great importance in the open public hearing process. The insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many topics, there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore, please speak only when recognized by the chair. Thank you for your cooperation.

I will point out that you do have time allocated for your presentation, and you will receive

a warning and then a stop signal. And when you see that, please stop. Otherwise, you will be reminded as to your need to stop.

So with that, we will move on to the presentation by Dennis Carlton and Frederick Flyer with Compass Lexecon.

DR. CARLTON: Thank you very much for the opportunity to address the panel about our study. This study was funded by Lorillard. I should also mention it was done through the consulting firm of Compass Lexecon, and Compass Lexecon has worked on numerous matters other than this one for a variety of the cigarette companies.

My name is Dennis Carlton. I'm associated with Compass Lexecon. I'm also an economics professor at the University of Chicago. My co-presenter, Rick Flyer, is a PhD and an employee of Compass Lexecon and the principal investigator in this report. Let me take you through a brief summary of the report and urge you to consult the report for more details.

The purpose of this report is to assess the

likely effects of a ban on the sale of legal menthol cigarettes. There are four main findings.

If there were a ban on menthol sales then, first, current menthol smokers largely would turn to the black market to purchase their menthol cigarettes or, alternatively, will purchase non-menthol cigarettes in the legal market.

Second, black market cigarettes currently exist and likely would expand quickly in response to surges in demand for menthol cigarettes created by the ban.

Third, therefore, a ban will not eliminate most of the cigarette consumption by menthol smokers in the United States.

Fourth, the ban may have the unintended consequences of increasing criminal activity and allowing greater youth access to unregulated cigarettes.

Let me briefly take you through some of our analysis. Currently, menthol smoking comprises about 30 percent of all smoking. It would be a mistake to think that a ban on legal sales of menthol cigarettes

would lead to a decline in smoking of 30 percent. There are two important reasons why it's a mistake.

The first reason, and I think the most important one, is that a black market for menthol cigarettes will expand and enable many menthol smokers to continue to smoke menthol cigarettes. Now, why do I say that? A ban on menthol sales of cigarettes can be thought of as a tax, a very high tax, indeed, an infinite tax on legal sales of menthol cigarettes. But we have experience with actual cases of high taxation. When governments impose large taxes, it creates financial incentives for buyers and sellers to use a black market to avoid paying the tax.

We see examples, and we go through those in our report, and I know other people have submitted reports on such things. And in the report, we talk about Canada and New York. Let me just briefly talk about Canada.

In Canada, in the early 1990s, there were very large increases on taxes on cigarettes, and what that did was it led to a large and rapid increase in

the black market. Estimates are that, in Canada, in 1993, black market sales comprised about 31 percent of total cigarette consumption. Canada responded by precipitously cutting taxes, and, sure enough, the black market fell precipitously. More recently, there have been some estimates that provinces in Canada, in particular Quebec and Ontario, have black markets of about 40 to 50 percent.

I said there was a second reason, and that is that some menthol smokers will switch in response to a ban to smoking non-menthol cigarettes purchased legally. In order to figure out how important this is, you need to have a statistical model of demand behavior, and we've tried to estimate that in the report.

In order to estimate the effect of the ban, you have to estimate the magnitude of these two responses I've just discussed. And in order to do that, you have to ask the question, what will happen to the effective price of menthol cigarettes in the black market?

That's a hard question to answer. But you

can do some calculations that will give you some insight into what might happen. And let me just say by the effective price or full price, what economists call full price, I mean that price that reflects the factors influencing consumer purchase decisions in the black market.

So, for example, using our estimates, if we assume that the effective black market price of menthol cigarettes will be, say, 25 percent higher than the current legal price, our estimates indicate that menthol sales in the black market will be about 72 percent of current menthol sales. Total smoking, menthol plus non-menthol, will initially fall by about 2 percent.

Now, of course, these numbers depend on what you're assuming about the effective price of menthol cigarettes. If instead of the 25 percent increase you assumed it was 50 percent, then these numbers would change. The black market would be not 72 percent but would be 56 percent of current menthol sales. Smoking would fall not by 2 percent but by 3 and a half percent.

But however you interpret these numbers, it seems pretty clear that even large increases in the effective price of menthol cigarettes in the black market are going to lead to the existence still of a large black market. These estimates indicate that black market sales and lost tax revenues will be in the many billions of dollars.

Now, whenever you do a study, I think you should always put forward the caveat, especially to an organization, a body like this that's trying to make a decision. It's hard, as the earlier speaker indicated, to have detailed information about black markets. Predicting the effect of price in a black market is difficult. Second, our estimates of switching behavior could be refined with better data. We used the data we had, but that could be made more precise.

Finally, I want to emphasize that we do not study, in our report, the effects of a ban on youth initiation or long-run effects. We're giving you the annual, the initial annual effect. And, obviously, youth initiation and long-run effects are two areas

deserving of future study.

Let me just finally turn to some unintended consequences. To the extent that a black market develops and expands, obviously there'll be a growth in criminal activity. Second, unintended consequence of a ban might be increased youth access to unregulated cigarettes. What do I mean by unregulated cigarettes? Counterfeit cigarettes, cigarettes sold in locations where age restrictions on the consumer are not enforced, locations where advertising and promotional decisions aren't restricted as they are when you buy cigarettes right now through a legal channel.

So that's been a very quick summary of the report. I urge you to, for details, consult the report, and I'm happy to answer any questions about either the presentation or the report, and I'll be answering questions with Dr. Flyer. Thank you very much.

DR. SAMET: Thank you for your presentation. Let me just ask one question, in a sense ground truthing your model and your assumptions.

I think you said that as much as with your 25 percent scenario, 72 percent of the sales could move to the black market. That actually would represent approximately 20 percent of cigarettes consumed in the United States in the black market.

Does that actually seem realistic to you as a plausible estimate?

DR. CARLTON: That the black market sales could be as high as 72 percent?

DR. SAMET: No, that it would represent 20 percent of the U.S. --

DR. CARLTON: That it could be? Well, you know, if you look at the Canadian experience, in Canada, in Ontario and Quebec, it's been reported just recently, over the last few years, that the amount of black market sales is somewhere between 40 and 50 percent. So those numbers do sound pretty high, and you wonder how that could happen. But apparently it has happened.

Also, in Canada, in the early 1990s, as I reported, they estimated that 31 percent of all consumption of cigarettes in Canada were black

market. So numbers like that, though perhaps initially sounding mind-boggling, appear to be consistent with the facts.

It's also true that in one of the other submissions I saw, I believe by Philip Morris, there were estimates as to black market sales in states along the Mexican border. And, again, those were in the range -- I don't have all the numbers in my mind, but I think they were in the range of 20 to 25 percent. So, yes, large amounts of sales in the black market I think are possible.

DR. SAMET: Right. Except, again, I think just as we -- these estimates will be helpful. I think the distinction with the scenarios you mention is that we're talking about a product that is otherwise banned as opposed to conventional cigarettes, which is what we're talking about here, which is just why I raised the question. But let me turn to others.

Jack?

DR. HENNINGFIELD: I had the same question because 72 percent is about providing someplace

around I think 70 billion cigarettes to 14 million people. But the real issue that I think your presentation raises, to me, is the importance of not just making some assumptions, but for FDA to develop various models, various scenarios, to see what is plausible and what kinds of scenarios could be affected through appropriate controls and with surveillance.

The Canadian experience keeps coming up, but the Canadian experience, to provide all those cigarettes, my understanding was, took the cooperation of R.J. Reynolds providing cigarettes across the border. And so that didn't just happen with small-scale contraband production and distribution, so I'm not sure that's relevant here. But, again, I think we need models, scenarios, and what leaks could be plugged with oversight.

DR. SAMET: Karen?

MS. DELEEUW: In your presentation, you rightfully noted that a 30 percent decrease in menthol smokers would not result in a 30 percent decrease in smoking, and you mentioned switching to

non-menthol and the black market.

What assumptions did you make about people who might choose to quit as a result of the ban?

DR. CARLTON: Well, the quitting behavior was based on a price sensitivity of about -- I think it was .3 we used for menthol, so that you don't get, at least initially, based on these aggregate estimates of demand that are in the economics literature, a large decline in smoking when prices go up even by the 50 percent. Let me make sure. Let me just clarify.

Even though, when prices go up by 50 percent, I said that the market was -- I think it was 56 percent of the legal market. What I'm indicating is that is nothing like eliminating the market; 56 percent still remains. And so that was one of the bases we used for quitting.

DR. FLYER: Let me add one thing. The actual level of quitting will depend on the black market. So if the black market comes in with a robust supply such that menthol cigarettes are priced similarly to their current levels, there will be very little

quitting. If the menthol supply is -- let's say there's large enforcement efforts that actually are able to restrict the menthol supply, what that means -- that's why we're using these different assumptions about what's called the effective price.

An enforcement level that's effective will have a large impact on the price because it's really going to reduce the supply of cigarettes. As you reduce the supply, the black market price will go up. So if there is success in reducing the supply of menthol cigarettes, that would lead to higher -- and affect the price, which would lead to higher decline rates. And we document this in the report.

As the effective price goes up, we document what effect that would have on aggregate smoking. Fifty percent would have about a 3 and a half percent effect on aggregate smoking in the U.S. If it went up to, let's say, 100 percent -- we could do the calculation; I can't do it here as I stand, but it would be somewhat higher than 3 and a half percent, maybe 5 percent, 6 percent. You could use the methodology in the report, and you could actually

calculate, at different price levels, what the effect on aggregate smoking would be.

DR. SAMET: Cathy?

DR. BACKINGER: That was my question.

DR. SAMET: Okay. Mark?

DR. CLANTON: When you made your comment about ban on menthol cigarettes being a tax, and, in fact, potentially being an infinite tax, I started to think about the data out there on price elasticity of tobacco. You must know a lot more about this than I do, obviously, but there are a number of studies that show that the price elasticity of tobacco is slightly negative; that is, as price goes up, to some commensurate amount, there is a reduction in sales. In fact, I think most of the studies range from if you have a 10 percent increase, you get either a 1 percent decrease, all the way up to a 15 percent decrease based on elasticity. That's been calculated.

So when you said an infinite tax of a ban, you obviously didn't mean to imply there's sort of an infinite negative elasticity, meaning that would be a

huge and massive decrease in the sales of tobacco, really, across the board because I think you talked about -- you calculated an increase in the cost of black market tobacco as well.

So I just wanted to understand what you meant by that.

DR. CARLTON: Sure. Let me clarify that because that's actually a very good question.

By an infinite tax, I'm not talking about the elasticity. I'm just saying the government -- you can think of a ban as someone walking into the store and saying, you can buy this good, Dennis, but you've got to pay a tax of a trillion dollars. So I walk out of the store. That's equivalent to a ban.

In order to figure out if you don't have an infinite tax but a tax of, say, 50 percent, then you do need to know my sensitivity, my price sensitivity. And you talked about elasticities; the range in the literature for the aggregate elasticity, typical range that's cited, is between .3 and .5. And what the means, as you say, not that big. That's the whole point of the problem.

If the elasticity isn't big, that means that there's going to be a large black market. Why? What's the intuition? The intuition's pretty clear. You have a product that people are consuming here, and they crave it. They're like addicted to it. Okay? And now I say, I don't want you to buy it. What's the response going to be? Huge demand. They're going to be searching out places to buy it. It's going to create these financial incentives for people to create a black market. That's the problem you're facing. That's exactly right, so that's a very good question.

DR. FLYER: Let me add one thing. There's --

DR. CLANTON: And you were completely responsive to the question. One of the differences in the paradigms between, again, your analysis, which I don't have any problem with at all, is that we actually have, by virtue of statute, a requirement to look at public health, an effect on public health. So I wanted to make sure we didn't lose that. Even at the margin, a 10 percent, 15 percent, 30 percent under negative .3 elasticity, a 10 percent increase

would give you 3 percent and even higher if it were a total ban.

We need to understand what an impact on public health that would be. We understand it's not 30 percent, but it could be a really big number. So I understand your analysis, but also understand we have a requirement to look at the public health effect of the ban.

DR. FLYER: I understand. But just one clarifying comment, and that is, when you look at it as an infinite tax on legal supply, it's only raising the legal price. The studies you're referring to are looking at raising all cigarette prices simultaneously.

So here, what we have to do, the calibration essentially is what we do, is we take the industry elasticity of between, as you mentioned, .1 to 1.5, which would translate to the numbers you gave, and we say, okay; how does that look different here when you have these two other options, because you have some of that demand that would dry up.

If you could raise the price of cigarettes to

infinity, nobody would smoke because nobody could purchase a pack of cigarettes. So we say, okay. But in lieu of legal menthol cigarettes, you're going to have non-menthol alternatives and black market menthols, and the real price effect is what's the price of the black market menthol. And that's really the price increase that you have to calibrate when you're looking at this problem.

DR. CARLTON: But it is -- I just wanted to add -- I tried to get it on the slide but the slides don't work any more. We do calculate the overall effect on total smoking, which was, for the 50 percent price increase, 3 and a half percent, and it was -- I can't remember the number I had up there. Oh, okay. Thank you. It was 2 percent for a 25 percent increase.

So that's the effect on total smoking, the decline in total smoking, from our experiments.

DR. SAMET: Neal?

DR. BENOWITZ: I've got some comments both for you and also for the whole issue of black market.

The assumption of no alternatives when you

switch is based on the fact that taste is immutable. We know that the biggest taste change was when we went from the old style, nonfiltered, plain old cigarettes to cigarettes that were filtered and ventilated. And at first people didn't like them, but then eventually there was no black market and people just switched to cigarettes.

I think a big part of it is marketing. You market it and that's what's available. And when you stop marketing menthol cigarettes and nothing else is available, why wouldn't we just do what happened with light cigarettes? Why do you think that the taste is so immutable that people are going to black market cigarettes?

DR. FLYER: I think that's a good point. And one caveat in our study -- and I'm not sure if it was in our caveats -- is we're measuring short-run responses, and the long-run responses may be much different. So if tastes are immutable, more smokers may switch to non-menthol than we're predicting.

DR. SAMET: Just a question. You mentioned, I think, as your last point, about unintended

consequences of increasing criminal activity and allowing greater youth access. These seem to be perhaps qualitative conclusions.

What was the basis for reaching those?

DR. CARLTON: I would agree with your characterization of them as qualitative.

DR. SAMET: Yes. Was there any --

DR. CARLTON: Quantitative analysis was based on our comments --

DR. SAMET: Yes. And in terms of the youth access, is there any particular data that you would cite as suggesting that black markets increase youth access?

DR. CARLTON: That black markets increase youth access?

DR. SAMET: Yes.

DR. FLYER: In the report we cite smoking rates among adolescents in Ontario and Quebec, where the black market was rampant. And those smoking rates increased relative to other provinces in Canada. Whether that was due to greater access or other social phenomena, the report doesn't make that

distinguishment, distinction.

DR. SAMET: Melanie?

DR. WAKEFIELD: Yes. Your model seems to assume that black market menthol cigarettes could be widely distributed and fairly immediately available after a ban occurs. And yet the previous speaker was, I think, suggesting that contraband menthol cigarettes would be very easy to -- well, would be easier to detect because of their nature, and therefore enforcement efforts could be fairly successful.

In light of that, how would you reflect on that, on some of the comments made by the previous speaker in reflecting on your model?

DR. CARLTON: Well, I think that that point is probably a correct one about enforcement on counterfeit if it said menthol. However, I actually found the presentation -- I think someone referred to it earlier as disturbing, and I think it was -- that's how I found it also. I mean, it was an excellent presentation, but the range of ways in which you could avoid this ban on menthol cigarettes,

I thought, is much more detailed than we go through in our report. So we don't explicitly try and model these alternative ways of avoiding the ban either legally, by calling them cigars, or illegally, perhaps, by the mentholization process that he talks about.

To the extent that there are legal ways to avoid the ban, obviously that would lead to a growth in criminal activity. But it would still have this enormous effect that the ban wouldn't be effective, which is what we're trying to document, or how ineffective it could be. But in terms of detecting some counterfeit, that's quite possible.

It is also true, though, that the incentive for counterfeit and the incentive to sell on the black market, I suspect, could be very high in the short run for the reason I stated, namely, people want the good. And at least in the short run, the addictive properties of the good will cause them to be willing to pay high prices, and that'll create a financial incentive.

DR. SAMET: Tim?

DR. MCAFEE: I have a couple questions for you around this. First was just a clarification that it seems like your model is assuming, in the way it's working mathematically, that it's increased price due to switching over to black market accessibility would result in people quitting. I would make the assumption -- and I think implicit in some of the assumptions of even the whole concept as it was originally proposed were that there are other factors that might influence people.

For instance, somebody who's a law-abiding 45-year-old citizen who doesn't break any laws, has no interest in breaking laws, and is suddenly confronted with the fact that if they want to keep using their current brand with menthol, they would have to become a law-breaker, that some fraction of those people -- regardless of what the price was -- even if the price was identical, some fraction of those people would choose to not become a lawbreaker and would either change brands or quit.

So I'm curious. I realize it would be hard to make a quantitative estimate.

DR. FLYER: That's a fair point. And that's what, really, we maybe should have distinguished what effective price is. Effective price isn't just a monetary price, but it's also the inconvenience of getting the cigarettes and maybe the -- we'll call it the psychic costs of purchasing an illegal cigarette. And for some individuals, that psychic cost may be sufficiently high that their effective price could be 3, 400 percent higher than the legal price even though the monetary price may be very close.

DR. CARLTON: So what you're saying -- I agree with Rick. I agree exactly with your comment. So when we talk in the report, and I quickly referred to it as the full price or effective price, that's the price that best represents what it is that is influencing consumer behavior in the black market.

So if, for example, just to take a simple example, suppose the black market is all the way on the other side of town so you have to incur extra transportation costs? You would count that in. Or, as you say, suppose there's some fraction of the population that's not going to have anything to do

with an illegal purchase? That then would mean, for that part of the population, the effective price would be high.

That's why it's hard to predict what the -- and which I mentioned, that it's hard for me to come up with a very precise estimate of the black market price, the effective price. But we do know from experiences around the world that it's not so high that it's dissuaded large black markets from occurring.

DR. MCAFEE: So the reality, though, is the price and utilization, it might be that the actual utilization of the black market might be smaller. You'd still have an effect that you'd create, but there wouldn't be as many people that would actually be purchasing.

DR. CARLTON: Yes. That's correct. Or another way of thinking about it, whatever you think the monetary price is in the black market, add something to it, and that's what people will be reacting to in predicting the consumption behavior because of some of the reasons mentioned.

DR. SAMET: Okay. I think, actually, we probably should move on. Appreciate your presentation, and as for any model, we could probably discuss this a long, long time. I think it was a helpful discussion. Thank you.

DR. CARLTON: Thank you.

DR. SAMET: We'll move on to our next presentation, which I guess is number 3. Jim Tozzi, the Center for Regulatory Effectiveness.

MR. TOZZI: Good afternoon. I'm Jim Tozzi with the Center for Regulatory Effectiveness. We're a regulatory watchdog that's funded by most industrial sectors, including the tobacco industry.

We have completed, per our earlier testimony, a detailed report on contraband. It's being reproduced and it's going to be transmitted today -- it's probably up on our TPSAC website in the next hour -- on contraband.

I want to leave you with one point within the six minutes, and it's this. I think the committee has a very serious omission in its work plan, and I think the serious omission is this. It's not

something that I came to four months ago when I looked at contraband. And it's not the issue of most economists, was I wanted to start looking at the tax consequences of contraband. Really, it's the issue that Dr. Clanton said. What is the public health impacts of contraband? I'm not talking about the size. I'm not talking elasticity of demand. I'm talking your language, not mine. What is the health effects?

Now, if you look at that and start looking at the data on the health effects of contraband, let me first use a term that you use a lot. You use the term subpopulation. And there's two targeted groups in contraband that'll be affected by contraband health effects. And the two subpopulations are adolescents -- and why adolescents; because there's no vendors in the contraband market that ask for age checks when you buy contraband -- and a second is African Americans because of their large consumption of menthol.

Now, what are some of these toxic effects? And we started on the economics, and soon when I got

into the data, it was the health effects that seemed to pop out at us way more, and very serious as the economic effects were the health effects.

Now, as you know, constituent levels in itself doesn't suggest harm. But magnitudes, orders of magnitude in differences between legal cigarettes and illegal cigarettes, suggest some cause for concern. Let me take not my data; these are all federal data.

CDC says cadmium is two to six times as high in contraband cigarettes as authentic brands; thallium, 1.5 to 6; and lead, 3 to 14, an order of magnitude higher by the CDC. Tar and nicotine; ATF says it's 75 percent more tar, 28 percent more nicotine, 63 percent more carbon monoxide. And then in many cases, the counterfeit cigarettes have found to contain rat droppings, camel dung, sawdust, and tobacco beetles.

But in any event, that is some of the -- now, the question is, what does that mean in terms of health effects on those groups? And I'll address that in a second. But your statute says that you

also have to look at the impacts on nonsmokers. And if you look at the literature done by ATF, GAO, and the Justice Department, they all report in some detail -- and all of these in our report -- that cigarette traffic is a very, very substantial amount of revenue for terrorist organizations. Not my data. They're all in our report. ATF says it, Justice Department, and others say it. In addition, they say that established channels for contraband, whatever they are, can be expanded with not a lot of difficulty.

So where does this leave me? I think that the committee, by statute, has to look at the health effects of contraband. And the problem is -- and this is your field, not mine -- I could not find very much information except for one study that was published in the Journal of Nicotine and Tobacco. It was an Australian study by Dr. A-i-t-k-e-n that established and codified and enumerated at length the impact that contraband cigarettes had on adolescents in terms of mental retention, in terms of initiation, a whole lot of activity. So I suggest that the group

look at this.

Now, is that a valid recommendation when you have this commitment of March 31st? As they say in New Orleans, that ball don't bounce. You cannot make March 31st and do the study that I think is required.

So what do I suggest? I suggest you issue, then, an interim report, and that you issue an interim report and you address this important issue. I think it's imperative that a health committee looking at tobacco and specifically directed to look at contraband must examine the health effects of contraband, particularly in light of the available data. I must add, 50 percent of the students in Ontario that smoke cigarettes are contraband.

Thank you.

DR. SAMET: Thank you. Questions?

[No response.]

DR. SAMET: Okay. Thank you.

So we'll move on to our next presenter, Geoffrey Curtin from R.J. Reynolds Tobacco.

DR. CURTIN: Good afternoon. My name is Geoff Curtin, and I'm a principal scientist with R.J.

Reynolds Tobacco Company. And today I'd like to briefly summarize some emerging science on population-level effects associated with menthol versus non-menthol cigarette use and to address some misrepresentations made during the November meeting regarding the July industry findings.

So I'd like to speak to you specifically as the national survey data, as provided during the July meeting by the industry, indicating no adverse population-level effects associated with menthol versus non-menthol cigarette use have been confirmed and extended by other researchers. And the continued discussion of menthol preference diverts necessary attention from our relevant findings that adolescent smoking prevalence is declining.

So these are the findings that we presented in July, which we based our no adverse population-level effects conclusions on. These were each looked at by a number of studies recently published in the journal Addiction, 11 different studies that used national survey data from the TUS-CPS and NHIS.

When you look at those studies -- and I've

been very inclusive here, so it's included studies that do agree with what we said earlier and which do not -- in terms of older average smoking initiation age, including among blacks and females, it was confirmed in all three studies that looked at this metric. Our finding of lower average smoking intensity, including among blacks and females, was confirmed in three of five studies, with no differences in the remaining two studies. And these results were extended by reporting no differences in time to first cigarette, whether it looked at 5 or 30 minutes, in three studies.

In terms of our finding of higher percentage of adults attempting smoking cessation, that was confirmed or no differences were seen in three studies, including and extended to no differences for quick duration and lifetime quit attempts. And no age-related differences, including young adults, were confirmed in two of the three studies that reported this out. There was a single study suggesting an age-related effect, but the referent was 65-plus years.

In addition, there was a recent presentation at the 2010 APH meeting, which I'm sure many of you are aware of, by Dr. Caraballo and his people looking at menthol and nicotine dependence in the NHANES. They reported no age-related trends, including among young adults; a lower smoking intensity and smoking duration, which they argued was a dependence metric; no differences in time to first cigarette, or nicotine dependence score; with their overall conclusion being no differences in dependence levels between menthol and non-menthol cigarette users.

If you go back and look at the work that was presented by Dr. Hersey in the November meeting, the two national studies that looked at dependence by Dr. Hyland, both came to the same conclusion of no difference in dependence. So we would argue, by any measure, the results that we showed the committee in July have been confirmed and extended by other researchers using national survey data.

Much was made of our presentation or our conclusions on the NSDUH and age-related trends in the November meeting, leading one to believe that we

came up with different results than Dr. Giovino or that our method was flawed. Both would be incorrect.

We created data or came up with data that was very similar to what Dr. Giovino presented, but we had issues with that data, and these were the issues that we talked about at the meeting. One is that it was suggested that this was the only survey -- that is, the NSDUH data was the only way to look at menthol. As I just pointed out, the APH poster confirmed that the NHANES is available to do this analysis and confirmed no age-related trends, including among young adults.

We had an issue with the identification of current smokers based on an overly-inclusive smoking categorization as being inappropriate for trend analysis. We have done some additional work in that area, and we've found that the age-related trends do not appear to change over a range of smoking categorizations. I can go into that in the clarifying questions section. And we argued that menthol preference was not necessarily based on usual brand.

This issue, in our opinion, remains, as brand data are routinely not used to assign menthol status for published analyses. In any case, menthol preference is not informative, although argued to be in November, in terms of menthol status during smoking initiation or addiction.

In terms of how menthol status is assigned with the NSDUH, in the NSDUH report, menthol status was assigned by a specific single question, much like we argued we did in July. And in Dr. Caraballo's presentation in March of 2010, he specifically said he used a single question: Were the cigarettes smoked during the past 30 days menthol; yes or no? He specifically said he did not use brand information, as there was some branding issue, and the use of this single question was recently confirmed last month in his manuscript published in Nicotine and Tobacco Research.

The only other paper we could find that's looked at NSDUH and menthol was a Crestlake 2008 paper, which was fairly unclear exactly how they did it. If in fact this survey is so easy to use, to use

brand information to address this issue, then why has it so rarely been published, and why does almost everyone seem to use the single question we used?

We would argue that smoking prevalence is much more informative and that this debate on smoking preference is misleading. There are data showing statistical declines for adolescents', male and female, smoking prevalence. Dr. Giovino extended those two declines for menthol and nonsmoking prevalence. There's also data suggesting decreases in initiation rate. We gave some of that data as well, based on menthol and non-menthol smoking, at the last meeting.

So to conclude very quickly, industry findings were confirmed and extended recently. Preference data is not informative in terms of menthol status during initiation and addiction. Our industry findings are appropriate and consistent with the published studies. However, this continued assertion that adolescent menthol cigarette use is increasing misrepresents the available data. And I can speak to that more during the qualifying

questions. Thank you.

DR. SAMET: Thank you for your presentation.

Questions or comments? Mark?

DR. CLANTON: On the issue of smoking in African Americans, you would certainly agree that African Americans smoke almost completely, 80 percent, mentholated brands. You'd agree with that.

DR. CURTIN: I agree with that, and that's the data we presented back in July. And I don't think I've seen anything since then that would lead anyone to question that.

DR. CLANTON: On the issue of studies showing no effect on health, I want to ask you a little bit about that. In the most recent Addiction monograph, there's at least one study looking at the health profiles of mentholated smokers versus non. And they agreed that African Americans actually smoke fewer cigarettes, which is a point I think you brought up earlier. But their conclusion on health was that although they smoke fewer cigarettes, their health outcomes are identical to those people who smoke more cigarettes.

So do you think that's still a non-effect, that they still get lung cancer and other diseases at the same rate as those who smoke more cigarettes?

DR. CURTIN: I am familiar with the Addiction paper. It's not what I focused on because I was looking at population-level effects and not individual harm. But I also know that there was a couple papers just published, including by Dr. Benowitz and by Dr. Ashley, looking at carcinogen exposure, menthol versus non-menthol, and if there was any correlation. And, apparently, the findings were no correlation. In fact, I think the paper from Dr. Ashley and his colleagues used NHANES data, which also allowed for sample collection, and actually found lower levels of NNAL with menthol smokers, which was nearly statistically significant.

In terms of why the risk would be different, I think there's a number of variables, that would include genetic predisposition and other things that have been talked about in the literature. But, again, my talk was specifically about population-level effects. I am aware of the health risks

information. In fact, I think at the November meeting, in addition to Dr. Hyland's presenting no difference on dependence for national data, I think there were also two presentations that Dr. Hersey talked about that also suggested no difference in disease risks between menthol and non-menthol smokers.

Given the way Dr. Hersey presented the data, I don't remember if he stratified it out by race/ethnicity. I think he gave pretty much top line views. But I think it goes towards showing that there just aren't that many differences.

DR. CLANTON: And I would agree. It appears that there aren't any differences in health outcomes. Again, at some point we're going to have to unpack this issue about if you smoke fewer cigarettes but still have the same rates of lung cancer, diabetes, cardiovascular disease as those who smoked more, we're going to have to understand that.

But I do understand that we may not be able to trace back through pathways and toxins precisely why that's the case, which I think is the literature

you're referring to. But having the same rates of disease and smoking fewer cigarettes is at a population level, because the study I'm referring to looked at about 30,000 people at a national database. We're going to have to unpack that and be careful when we say no effect or no difference.

DR. CURTIN: Yes. We also need to think about what the differences in cigarettes are. I mean, we're not talking about smoking 10 versus 20 cigarettes. At least in our analysis, we're talking about smoking two or three cigarettes' difference, I think, at the max. And I don't remember what that demographic was.

I know when we were researching for our manuscripts, we took a look at some of the health effects data, and there were at least two reports, including by the Spitz group at M.D. Anderson, showing reduced lung cancer rates for menthol versus non-menthol smokers.

DR. CLANTON: Among African Americans?

DR. CURTIN: The Spitz publication was an African American-specific model showing reduced lung

cancer rates from menthol versus non-menthol smokers.

DR. SAMET: Cathy?

DR. BACKINGER: So you said in the presentation summary that "preference data is not informative in terms of menthol status and diverts attention from finding that adolescent smoking prevalence is declining." And I know you said that based on asking whether you smoked menthol in the last 30 days. But the report we heard earlier today from Dr. Hersey that used tobacco industry documents basically stated that the reason that smoking prevalence among adolescents is going down, it's among non-menthol smokers, and then presented brand information to show that. And I'm just wondering how that jibes --

DR. CURTIN: It's my understanding -- because I was listening closely to that. It's my understanding that what was presented earlier today was a summary of data that has been published, NSDUH data. And that's the survey we're talking about here. So I don't know that that was actual independent research by the tobacco company other

than recognizing what's been published. And I think Dr. Hersey has said for quite some time that there's an age gradient.

We don't disagree that there's necessarily an age gradient in NSDUH. But recent findings from NHIS, from TUS-CPS, and our own finding from NHANES, don't show an age gradient. Now, we'll give you that only NHANES looks at adolescents and adults. But the truth is, when these data were presented in November, it wasn't just an adolescent step effect. This step effect also influenced young adults 18 to 24 years old. We don't see that in any other survey except the NSDUH. That is our issue with the NSDUH.

If I can say one more thing, please.

DR. BACKINGER: Yes.

DR. CURTIN: When look at the preference data in NSDUH, whether you take Gary Giovino's approach of using brand data or you don't, you come up with a preference number of about 33 percent. That's 6 to 7 to 8 percent higher than is provided by NHANES, NHIS, TUS-CPS. So there still seems to be some of this misclassification that was brought up earlier, this

18 percent or what have you that's going on in that survey. We wish we understood it. We'd love to use the brand information that NSDUH provides. But we just haven't been able to do that effectively, and I don't think a lot of people have.

DR. BACKINGER: I guess I was just trying to get at the fact that you were making one statement based on the NSDUH data that didn't jibe with an earlier presentation that used the same NSDUH data to show something different than what you were saying.

DR. CURTIN: Okay. So you started the question by saying I'm arguing that preference data -- in other words, what someone's currently using right now -- is not necessarily informative in terms of what they started smoking with and if they are going to be subsequently addicted, more or less addicted.

I don't know that anything that was provided in the presentation this morning contradicts that. I think that during the qualifying questions session in November, there was a leading question that said, is the data you're presenting, Dr. Giovino, consistent

with it may do this? And his answer was, it's consistent with it, but it doesn't directly speak to it. It may be consistent with it. I don't know that Dr. Hersey said anything that goes against the statement I made.

DR. SAMET: Okay. I think, Neal, did you have a question?

DR. BENOWITZ: Yes. To follow up to Dr. Clanton's comments, there's a couple observations that have been striking to me with respect to the cigarette dose response, which seems to me is really different among African Americans compared to Caucasians. And we don't know for sure if it's menthol, but it certainly could be menthol.

That is, the consequences of being a light smoker for an African American seem to be different than Caucasian. In the Hayman lung cancer study -- I'm sure you know that study -- if you look at people who were light smokers -- I forget what -- if it was like up to 15 a day, or 10, or whatever -- the lung cancer risk was three times higher in African Americans compared to whites. If you go to

30 cigarettes per day, the risk was the same.

So clearly, there -- and then a lot of cessation studies done with African Americans show that African American light smokers -- not light cigarettes, but fewer cigarettes per day -- have a much harder time quitting than what we see in the same literature for white smokers. So there clearly is something about this dose response such that African American smokers who smoke relatively few cigarettes, and those are mostly menthol smokers, seem to have higher disease risk at low-level consumption, and at least by some indices, higher dependence measures.

To me, those are very striking observations. I don't know what your response is about that.

DR. CURTIN: I didn't really find a question in there. But what I will say is the data that I've seen at the national level suggests that these metrics of dependence -- we started with cigarettes per day because it's something we could look at quite easily, and it was our first pass. But the work that's been published since, showing no difference in

time to first cigarette or smoking duration or even dependence scores that was presented at the APH meeting, suggests, at the population level, no difference in dependence.

Now, we do recognize that there seem to be fewer cigarettes smoked per day, and why that would lead to different outcomes, that's beyond what we're looking in in our results.

In terms of dependence, same thing. The data that's come out since we first presented our national population data is that there seems to be no difference in dependence. I think Dr. Hersey spoke to it last November. If you look at the national survey data that he looked at, both studies by Dr. Hyland suggested no difference in dependence. Dr. Caraballo's work on NHANES, no difference in dependence. And the work that was just published in Addiction from NHIS and TUS-CPS, five, six, seven studies looking at different metrics, no difference in dependence.

Now, the clinic study, I addressed that issue in the presentation in July. I saw or noticed today

that there's a number of people that go through and stratify the studies, when they were going through and stratifying the industry documents on what was helpful that's not, as I explained in July, we did the same thing. And we didn't think that clinic data was as generalizable or as informative as national population data. And that's where we've really focused our activity. And luckily, there have been a number of reports since then, specifically in Addiction, that addressed some of the same issues we did.

DR. SAMET: Okay. Any other questions?

[No response.]

DR. SAMET: Thank you very much for your presentation.

DR. CURTIN: Thank you.

DR. SAMET: We'll move now to William R. True from Lorillard Tobacco Company.

DR. TRUE: Good afternoon. I'm Bill True, senior vice president of research and development at Lorillard Tobacco Company. And, once again, I appreciate the opportunity to address the committee.

Today, I'd like to present a summary of the weight of evidence before TPSAC regarding the use of menthol in cigarettes and risk to public health.

Epidemiology studies on menthol cigarettes and disease risk integrate all aspects of smoking, including all smoking behaviors, long-term exposure to smoke constituents, and duration of smoking history, which reflects both successful and unsuccessful quitting attempts. As such, epidemiology studies are particularly relevant in an evaluation of the health effects of menthol.

Epidemiology is also the foundation of all the surgeon general's determinations regarding smoking and disease, and it is very appropriate that TPSAC give careful and objective consideration to the substantial body of epidemiological evidence comparing the risks of menthol and non-menthol cigarette smoking.

We have previously discussed over a dozen peer-reviewed epidemiology studies reporting on the associations between menthol smoking and disease occurrence. Two additional studies were provided to

TPSAC in the briefing materials for today's meeting. These studies are consistent and show that the overwhelming weight of scientific evidence confirms that menthol has no effect on risk for lung cancer and other diseases associated with smoking. There is no sound scientific support for epidemiology for regulating menthol cigarettes any differently than non-menthol cigarettes.

Although some smoking behavior studies have attempted to compare specific elements of complex smoking human behaviors, biomarker studies are the most meaningful and quantitative way to measure the net effects of all the different ways people smoke cigarettes. There are over a dozen peer-reviewed studies reporting on the comparison of biomarkers of exposure between menthol and non-menthol smokers.

The majority of the studies, including studies recently published, report no increase in exposure to smoke constituents for menthol smokers. The studies reporting no difference include all of the largest and best-conducted studies from both academic and industry researchers. These results

from biomarker studies are completely consistent with epidemiology studies and clearly provide no scientific support for regulating menthol cigarettes any differently than non-menthol cigarettes.

With respect to an association between smoking and dependence and cessation, the weight of evidence, particularly the data developed from the largest and most representative study populations, does not show that menthol smokers are more dependent or that menthol impairs smoking cessation. As noted earlier today, the largest biomarker study to day of over 3500 smokers, menthol status had no statistically significant effect on the overall scores using the Fagerström test or on any individual item of the test, including time to first cigarette.

The studies that have been recently published or provided to TPSAC do not change the weight of evidence. For example, in the recent edition of the journal Addiction, as highlighted by Dr. Curtin a moment ago, several studies examining menthol smoking were published when using the data from the tobacco use supplement of the current populations served.

One study found no difference in lifetime quit rates between menthol and non-menthol smokers. Another found that menthol smokers start smoking at an older age, smoke less than non-menthol smokers, and had a lower percentage of time to first cigarette within 30 minutes.

When comparing subgroups or study participants, the reported dependence and cessation rots are often inconsistent, conflicting, and often illogical. For example, one study found that non-daily smokers were more dependent that daily smokers.

Therefore, dependence and cessation study results, notably those that are secondary analysis from studies designed to evaluate smoking cessation drugs in outpatient clinic settings, do not provide appropriate scientific basis to support regulating menthol cigarettes any differently from non-menthol cigarettes.

An independent third party conducted an analysis of the published studies on menthol and smoking initiation, dependence, and cessation based on the criteria developed by the Agency for

Healthcare Research and Quality in its report on tobacco prevention, cessation, and control. Due to their design, several of the studies analyzed are limited in their ability to assess relationships between menthol and these smoking behaviors.

In addition, these studies often lack the appropriate statistical rigor or clear explanations of the statistical processes used. Because of their study designs and study populations, many of these studies cannot be extrapolated to smoking populations in general.

In addition, the dependence and cessation studies typically do not report the tar and nicotine yields of the cigarettes smoked by the study participants. The nicotine and tar yields of the most popular menthol cigarettes are typically in the highest third of the marketed brands, while popular non-menthol brands tend to have lower nicotine yields. With the current reported data, we have not seen any analysis to determine whether any effect on dependence and cessation is due to nicotine rather than menthol or other factors.

Of the studies on menthol and smoking initiation, dependence, and cessation, in which the methodology was even marginally sufficient to support inferences related to menthol, only six studies made appropriate conclusions based on the data. Of these six, five found no difference in outcomes between menthol and non-menthol smokers.

All of these realities must be considered by TPSAC as it develops its advisory opinion on menthol. The ebb and flow of the popularity of a given cigarette brand or brand style in any free marketplace should not, and scientifically cannot, be taken as evidence for a cause-and-effect relationship between menthol and societal smoking trends.

In conclusion, I firmly believe that TPSAC already has before it the requisite sound, regulatory science base to develop and advance a defensible advisory opinion to FDA that menthol in cigarettes does not increase the risks to public health that are inherent in smoking. Thank you.

DR. SAMET: Thank you.

Questions? Neal?

DR. BENOWITZ: I'd just like to follow up on one statement that you made. You were talking about the fact that the menthol cigarettes are among the highest tar and nicotine yield, and suggesting that you can't separate out the menthol from nicotine effects. I assume that the reason that's the case is that menthol somehow allows people to tolerate more nicotine or makes them like it better. So there's some synergy between high menthol and high yield.

Is that a good thing?

DR. TRUE: Well, if you go back to our presentations in July, I could tell you that the menthol levels of Newport, for example, are on the lower end of the menthol levels that are in commercial products. Yet, the nicotine level of the full-flavor Newport product is up in the top third of nicotine levels. So I don't subscribe to your proposition that menthol is added necessarily to buffer those effects.

My point in talking through this issue is that when you look at the urban-centered cessation clinic studies that have been published that have

some mixed results, and in some cases have shown some difference in quit rates between menthol and non-menthol cigarettes, you may very typically be concentrating the effect of the nicotine yield as well as the other confounding factors of socioeconomic status and so forth that we've discussed previously. We would like to see there be a match study, if necessary, to be able to look at cigarettes of matched tar and nicotine with and without menthol before any independent effect of menthol is drawn as the conclusion.

DR. BENOWITZ: So just to follow up on that, why is it that the yields of menthol, the tar and nicotine yields of menthol cigarettes, are on average much higher than that of non-menthol cigarettes?

DR. TRUE: My point was that the tar and nicotine yields of the most popular menthol cigarettes tend to be higher than the tar and nicotine yields of the most popular non-menthol cigarettes.

DR. BENOWITZ: Yes. But why? Why?

DR. TRUE: I can't explain that.

DR. BENOWITZ: It's a consumer preference issue.

DR. SAMET: Mark?

DR. CLANTON: In the studies you referred to about biomarkers and measuring biomarkers, I guess as a proxy for toxicity, did any of those studies include nicotine blood levels? I ask that because nicotine blood levels is not normally associated as a biomarker of smoking. It is what it is.

Were any of those studies looking at or mentioning nicotine blood levels?

DR. TRUE: I'm not aware if they have been. We can go back and take a look, but I'm not aware that they have been.

DR. CLANTON: Well, I want to tell you why I ask, because it does appear clear, based on a number of studies; I mean, nicotine is metabolized principally through at least two pathways, glucuronidation and through a cytochrome 2A6 pathway. Both of those pathways are inhibited by menthol. So I wanted to understand if you were talking about nicotine blood levels, which can be higher in people

who smoke menthol, or if you were just looking at cotinine and more traditional biomarkers.

DR. TRUE: Well, I think the inhibition that you're describing in terms of those two pathways have been done in very small pilot laboratory studies, and I'm not sure have been confirmed by the actual biomarker data in large population studies.

DR. SAMET: Just a last comment. As an epidemiologist, I have to say that epidemiology has been central to the surgeon general's report, but hardly the only element of science that has supported conclusions. The most recent report, in fact, is on the mechanisms by which smoking causes disease.

Thank you.

DR. TRUE: Thank you.

DR. SAMET: Okay. We'll move on to the next presentation, which is Dave Bryans from the Ontario Convenience Stores Association.

MR. BRYANS: Good afternoon, and thank you for this opportunity to speak to all of you today. My name is Dave Bryans. I'm the president of the Ontario Convenience Stores Association, and I

represent about 8,000 convenience stores in Canada's largest province.

In my role, I work very closely with the National Association of Convenience Stores here in the United States, known as NACS, and I'm here today to provide insight on the Canadian experience with tobacco control and the growth of the illegal tobacco markets in our country. These markets not only harm our communities but also thousands of small family-run businesses. I think this information will be important as you consider going forward.

As you may know, Canada has historically been the leader in anti-tobacco legislation. However, you may not be aware that successive governments have focused on tightening regulations on the legal market, and they have fostered the creation of a massive underground illegal tobacco market, particularly in Ontario and Quebec, Canada's two largest provinces, where about 20 million people live and exist.

Despite their best intentions to help reduce smoking by policy-tightening regulations on the legal

tobacco market, policy-makers in Canada have created an environment that has allowed a massive illegal tobacco black market to thrive. These illegal cigarettes are often sold in clear plastic Ziploc bags in quantities of 200. They are sold through distribution networks established by organized crime groups or through stores set up on aboriginal reserves. Our own federal police force, the Royal Canadian Mounted Police, have now identified over 175 organized crime groups behind the networks that move and sell these products. They are sold on street corners and they're sold near high schools and public schools. The smugglers moving these products often use the same distribution networks in our country to traffic in illegal goods such as guns and drugs.

The Royal Canadian Mounted Police also indicate that 90 percent of all illegal cigarettes appearing in Canada are being illegally manufactured in the United States in factories set up within the territory of St. Regis and Akwesasne Aboriginal Reserves in New York State. That reserve straddles the U.S. and Canada border in our two largest

provinces, Ontario and Quebec, creating a smuggling corridor that is unknown anywhere else in the world.

To give you an idea of the size of the black market that has grown, independent research in Ontario has shown that the illegal cigarette market grew from 13 percent in 2006 to over 48 percent in the most recent survey data available. This means that one in two consumers have access to an illegal product. This means billions of cigarettes are manufactured and sold without regulations, without taxation, and without controls to prevent kids from accessing tobacco. Governments have lost billions in tax dollars. And anti-smoking programs, particularly those directed at our youth, are being significantly undermined.

We believe this is very relevant to the Tobacco Products Scientific Advisory Committee because the Canadian government's decision to significantly raise tobacco taxes and ban certain types of tobacco products has created an illegal tobacco problem, and in many areas is actually making tobacco products more easily accessible to all of our

kids. Smugglers don't check in Canada for ID.

Convenience stores certainly have a business interest, a very vested business interest, as our stores are one of the few regulated places where legal tobacco sales are permitted. However, we have an equal interest in acting as responsible community retailers. We take our duty of selling age-restricted products like tobacco, alcohol, and lottery tickets very seriously, and we do so with the utmost of care.

In Canada, we have demonstrated our leadership in responsible community retailing by developing world-class ID check systems. We use swipe card technology in terminals, where we read the driver's magnetic strip and verify the age for all of the employees.

Of course, kids should never smoke, and since 2007 we have extensively studied the problem of illegal tobacco and how prevalent it is amongst our youth. Through an independent research firm, we visited high schools and collected cigarette butts to determine youth access to illegal tobacco.

In our most recent study, 175 high schools were visited in Ontario and Quebec, and over 34,000 cigarette butts were collected and analyzed. Contraband cigarettes were found at every school, and at some schools in Ontario, the numbers were as high as 50 percent and over 80 percent, shockingly, in Quebec.

My message here today is that the committees such as this one should be mindful of the unintended consequences of tobacco control measures in the very complicated environment that has developed in North America. Canada's problem of illegal tobacco is directly tied to the United States. Illegal cigarettes are being manufactured in the billions within the borders of the United States. For the first time ever, in late 2010, we saw the telltale plastic bags begin to appear containing menthol cigarettes. Very first time.

Today the flow of these illegal cigarettes moves north into Canada because of market conditions created by government policy-makers. While their motives were well-intended, their failures to examine

how certain anti-smoking measures could enable the uncontrolled growth of the illegal tobacco markets are lessons for other jurisdictions.

Should the United States government move to implement the ban on menthol tobacco products, it should not be surprised to see the illegal tobacco manufacturing capacity that's already here exploit this new opportunity such a move would provide. The end result could be similar to Canada, where these products actually become more accessible.

Thank you.

DR. SAMET: Thank you.

Questions? Yes, Mark?

DR. CLANTON: It looks like, at least over the past three or four years, that the overall smoking rates in Canada have been coming down, coming down slightly; I know there are some provincial differences, but based on data of Canada in general, that they've been moving down.

How do you reconcile that with the fact that there are so many illegal contraband cigarettes on the market in Canada?

MR. BRYANS: Well, first off, I don't believe smoking rates. I think the health groups in Canada have already declared that smoking rates have totally flattened out and youth smoking is in jeopardy. So I think that's the issue we're facing. We all work together as responsible retailers. I don't think there's any retailer in this country, or any country, that wants people under 19 to get a pack of cigarettes. I mean, we're all parents first.

High taxation and banning of certain products has hurt the small business model in Canada. I can only speak from that. People have been leaving our stores in droves and buying them out of trunks of cars. Just think of how well-organized, when over one million people in Ontario a day have access to untaxed, uncontrolled government cigarettes delivered to their door with no advertising, no promotion, and hurts our business model.

Our customers don't come in and buy chips, they don't buy pops, they don't buy lottery, because they don't buy cigarettes as regularly. So that's what's happened, and it's because of aboriginal

production and government's unwillingness in Canada, and probably the United States, to go onto federal reserves, that there are some treaty rights, and take on all these illegal production facilities.

DR. SAMET: Tim?

DR. MCAFEE: Well, I mean, you certainly made a very convincing case that there's a profound deficit in adequate enforcement, probably both in Canada and collaboration between Canada and the U.S. I'm curious, again, why not start with that as the hypothesis as opposed to assuming that we should roll back policies that, again, both in Canada and the United States, have proven to be very effective?

MR. BRYANS: Well, I don't think I've ever asked to roll back policies. I think those ships have left the dock. But I can tell you, four years ago I asked the governments to help us with contraband, no different than coming to this committee. And they said, I'm your partner; we will fix it together. And here we are four years later at 48 percent, and everyone keeps getting this direction.

So I'm not here to ask you to roll back policy. I'm not here to ask you to change policy. I'm here to warn you that if we don't work collectively together -- and we've seen that in Canada; I just finished on my BlackBerry with the Minister of Revenue, trying to figure out how to fix contraband and communicate it in Ontario that it's an illegal, victimless crime that we have to correct.

DR. MCAFEE: So, in summary, we should pay careful attention to making sure that any regulatory changes that are made here in the U.S. under FDA jurisdiction should aggressively consider our options in terms of enforcement to ensure that we don't replicate the Canadian experience?

MR. BRYANS: Yes. You know, as interest -- and I'll just summarize that in Canada we have a flavor ban, but they did not ban menthol, knowing that this would create even a bigger black market. We can't control the market we have, let alone fueling it and growing it bigger.

DR. SAMET: Okay. Thank you for your presentation.

MR. BRYANS: Thank you.

DR. SAMET: Oh, okay. Sorry. I think we actually have one more question for you from the phone, from Patricia. Go ahead.

DR. HENDERSON: I just have a question. In many of the discussions that were presented today, there's been a lot of reference to how contrabands are going to be increased, particularly from markets of native communities.

There's 564 federally recognized tribes here in the United States, and there's just a small handful that are producing tobacco products. Of course, there's the one that you mention in New York. I truly believe that when we work closely with native tribes, we can actually address this issue, only because -- I say this because I'm native myself. And I just want to I guess speak for the rest of our native communities that are out there that we're willing to work with the government. I believe this is an issue that has faced our native communities for many years in terms of commercial tobacco.

But I always say, and I'll end with this,

that this is a word that we phrase all Navajo Nation. It's (speaks in Navajo), meaning that however we use tobacco -- we're talking about commercial tobacco -- it hurts the inner essence of anybody around you, near you, and, of course, yourself. And I just am hoping that if we're going to move forward on this issue, that we work very, very closely with our native communities. And I'm sure many of them are listening today and are willing to work with us.

MR. BRYANS: And I agree with that, and I'll just answer quickly. We all know in Canada -- and I'm not sure what it is in the United States -- that youth smoking is out of control on aboriginal reserves. It isn't the aboriginal people. In Ontario, we have 160 aboriginal reserves. What they're doing on their own land, in their stores and in their factories is actually sovereign land and it's legal. It's when it moves off that land.

So it isn't the people on the reserves that are benefitting from aboriginal production. There are a certain group, as the RCMP had pointed out and I said in my notes, that are using and hiding behind

aboriginal production to move cigarettes illegally around Canada. So it isn't the aboriginal people in general in our country. They actually live at a lower standard, and we have seen no marked improvement in their lifestyle because of the illegal activity.

DR. SAMET: Okay. Thank you.

MR. BRYANS: Thank you.

DR. SAMET: We'll move on, then, to Michael Weisman. And if you could let us know your affiliation, if any, please.

MR. WEISMAN: Yes. Good afternoon. My name is Michael Weisman. I am a member of the Boston law firm of Davis, Malm & D'Agostine. I paid my own way, including the $70.23 that I paid for my hotel room last night. I am a fellow of the American College of Trial Lawyers, a fellow of the International Academy of Trial Lawyers, and a visiting lecturer at Yale Law School.

Last month, a jury in Boston returned a verdict of $152 million against Lorillard Tobacco Company in a case entitled Willie Evans v. Lorillard.

I served as lead trial counsel to Willie Evans in that case, and thought that it would be helpful to talk a little bit about that case. I think it's important. Mr. Evans had planned to be here today, but was unable to come because of another commitment.

The evidence on which the jury's verdict was based bears directly on the issues under consideration here. Willie Evans brought the lawsuit in his capacity as the executor of the estate of his late mother, Marie Evans. Marie Evans died at age 54 of small cell lung cancer after smoking Newport cigarettes for 40 years.

She grew up in the Orchard Park neighborhood in Roxbury, where she received free Newport cigarettes when she was a young child. She received Newport cigarettes because they were handed out in and around the playground in Orchard Park. She traded them for candy with her older sisters until she was 13 years old, at which point she began smoking. She became a regular smoker at 13. She soon became addicted and was unable to stop, notwithstanding her many attempts to do so.

Ms. Evans' smoking history is entirely consistent with what we discovered about Lorillard's marketing plan for Newport and its use of menthol. Lorillard introduced Newport in test markets in late 1956. In a retrospective document, dated September 15, 1964, Lorillard described its plan for Newport as follows. The brand was marketed -- it says "marked," but it meant "marketed" -- as a fun cigarette. It was advertised as such and obtained a youthful group as well as an immature group of smokers. Newport was marketed successfully according to plan. It certainly was; Marie Evans was one of the people it was successfully marketed to.

In a June 1978 memorandum entitled, "Black Marketing Research," one of the central ideas mentioned in response to the question, how to reach younger smokers, is sampling, that is to say, giving cigarettes away to young people. And in an August 1978 memorandum, a Lorillard sales executive reported that, "The success of Newport has been fantastic during the past few years, and the base of our business is the high school student."

The jury heard a great deal of evidence about the role of menthol in the success of Newport. Notably, the jury heard, and apparently found persuasive, the testimony of Dr. William Farone, the former Director of Applied Research for Philip Morris and a consultant to the FDA, as well as the National Cancer Institute.

Dr. Farone testified that menthol eases the initiation of new smokers. He further testified that menthol gives you a cooling sensation that mitigates the harsh sensation caused by nicotine and other alkaloids in tobacco. I spent a great deal of time with Marie Evans while she was still alive, and she made it perfectly clear that when she smoked, menthol made it easier to start smoking and keep smoking. In this PowerPoint presentation there's some testimony from Dr. Farone, which I won't read because of limits of time, but you will have it.

After hearing three weeks of evidence and after deliberating for six days, the jury in the Evans case awarded $21 million to Willie Evans for the loss of his relationship with his mother and

$50 million to the Evans estate for the pain and suffering suffered by Marie Evans prior to her death. Then after hearing additional evidence and after additional deliberations, the jury awarded $81 million in punitive damages, bringing the total verdict to $152 million.

You may say these events were long ago. But in the punitive damage phase, Lorillard had a chance to explain to the jury what was different today. What they said was different today is that they are now heavily regulated. That brings me to you.

They did not say that their practices were different. They did not say that they no longer target youth. They did not say that they no longer thought that the base of their business was the high school student. They didn't say any of those things. What they said to the jury was, we are heavily regulated. That is what they said was different.

Just last week the trial judge ordered Lorillard Tobacco Company to maintain not less than $270 million of working capital in its business as security for the jury's verdict. The jury's verdict

reflected an appreciation both for the magnitude of the harm done to Willie and Marie Evans, and to the egregiousness of the conduct of Lorillard Tobacco Company in handing free cigarettes to children, particularly black children, in an effort to create a generation of smokers, knowing as it did that smoking was dangerous.

Before I came here today I met with another man who has throat cancer who told me that when he grew up in the Bronx in 1959 and 1960, he got free cigarettes because they were taped to the doorknobs of the apartment building in which he grew up.

Lest there be any confusion, menthol was an important part of Lorillard's strategy. There is an undated, unsigned memorandum in Lorillard's files entitled, "Why Menthol?", which reads in part, and I apologize for its offensiveness:

"Negroes, as the story goes, are said to be possessed by an almost genetic body odor. Negroes smoke menthols to make their breath feel fresh, to mask this real mythical odor." The document goes on from there and asks, "Isn't it really analogous to

the taste sensation of peppermint?"

The document, though undated and unsigned, closely mirrors Lorillard's marketing plan.

DR. SAMET: Please. Your time is over, please, so if you can come to a close.

MR. WEISMAN: I'm sorry?

DR. SAMET: Your time is up.

MR. WEISMAN: I can't hear you.

DR. SAMET: Your time is up. Please come to a close.

MR. WEISMAN: Okay. As counsel to Marie and Willie Evans, the best I could do was to try the case and ask the jury to award damages to my client. You can do much more. You can recommend that menthol be banned from cigarettes, and in so doing, take an important step in reducing the likelihood that children like Marie Evans will begin smoking, become addicted, and eventually die prematurely of illnesses caused by smoking.

DR. SAMET: Thank you.

Questions?

[No response.]

DR. SAMET: Okay. Thank you for your presentation.

Let's see. Our next speaker is Jitender Sidh. I hope I'm pronouncing that correctly. And if you could give us your affiliation, please, as well.

MR. SIDH: First of all, thanks for giving me time to speak today with the other guys. My name is Jitender Sidh, and I'm representing small, private retail business. It's Painters Mill Wine and Spirits. It's in Baltimore County, in Owings Mills, Maryland.

I would like to talk to you about, you know, we either mostly sell alcohol and menthol cigarettes. And we check legal ID there, and most of our customers are over 25 to 30s, you know.

If the menthol cigarettes are banned, I respectfully question why my customers should be penalized, and comprehension with those who will buy menthol cigarettes through an underground, contraband market, you know.

Second, I respectfully challenge the hypothesis that the best way to attack underage

smokers is to ban menthol cigarettes. As business owners, we share the commitment to preventing the youth access to tobacco. The facts are they're responsible, retailer, to verify the age of purchase. I'm not an expert in the black market sales or the street corner. But I find it hard to imagine that responsible black marketing entrepreneur will check a teen driver's license before selling them a baggie of menthol cigarettes.

Third, I would like to urge you to consider the fact that the victim of deceptive practice like black marketing, a store owner like me, would have the least ability to protect themselves or obtain a remedy.

In sum, I believe that a ban of menthol would only cost us more business and make it too hard to stay financially strong. It is not going to compel anybody to stop smoking menthol cigarettes. So it is loss and loss proposition.

Thank you for giving me opportunity to speak.

DR. SAMET: Thank you for your comments.

Questions?

[No response.]

DR. SAMET: Okay. Thank you very much.

MR. SIDH: Thank you, sir.

DR. SAMET: Our next presentation is by Anne Hartman from the National Cancer Institute.

MS. HARTMAN: I'm Anne Hartman, a biostatistician from the National Cancer Institute. I don't have any financial disclosures. Thank you for the opportunity to present to the FDA TPSAC members today.

I will present brand-new, nationally representative data on menthol smokers' intentions regarding what menthol smokers report they would do if menthol cigarettes were no longer sold. This is the first time this question has been asked in a large national survey. I will also report the most recent data on the percentage of current cigarette smokers that smoke menthol cigarettes.

The data come from the May 2010 Tobacco Use Supplement, abbreviated as TUS, to the Current Population Survey, or CPS. The CPS is conducted by the Census Bureau for the Bureau of Labor Statistics.

Each month, the CPS provides a large national probability address-based sample of households. I will present initial TUS weighted data from the first of three months of data collection. I am only presenting subpopulation data with sufficient sample sizes.

Among current cigarette smokers, the 2010 TUS asked, "Do you usually smoke menthol or non-menthol cigarettes?" For the sake of time, I will highlight the most important findings. From this table, we see overall that in May 2010, 30 percent of the general population of current smokers smoke menthol cigarettes. Among non-Hispanic black smokers, this is about 76 percent. Among females, this is about 35 percent. And among 18- to 24-year-olds, it's about 42 percent, decreasing with age.

Among those current smokers who reported usually smoking menthol cigarettes, the question was asked, "If menthol cigarettes were no longer sold, which of the following would you most likely do?", with choices, read in order that they appear here, "switch to non-menthol cigarettes," "switch to some

other tobacco product," or "quit smoking and not use any other tobacco product." Respondents could also indicate "none of the above," "don't know," or "refuse."

This table containing the May 2010 data shows that, overall, among all current menthol smokers, and considerable number, 39 percent, indicate that they would quit smoking and not use any other tobacco product. Further, among non-Hispanic black menthol smokers, 47 percent indicate that they would quit smoking and not use any other tobacco product. Looking at data by gender and age, we see that 42 percent of females and 41 percent of younger adults made this selection.

In summary, the reported levels of menthol cigarette use among current smokers in May 2010 are consistent with other national survey data. Most importantly, 39 percent of menthol smokers say they would quit all tobacco use if menthol cigarettes were no longer sold. The corresponding value is 47 percent for non-Hispanic black menthol smokers, and was also a considerable level for younger adults

and for females.

In conclusion, given that the available research indicates that behavioral intentions are generally associated with actual behavior, the results I have just presented suggest a potential substantial reduction in tobacco use if menthol cigarettes were no longer sold.

Note, in particular, the non-Hispanic blacks disproportionately smoke menthol cigarettes and suffer from tobacco-related cancers. Thus, their intention to quit all tobacco use if menthol cigarettes were no longer sold may yield a large effect on this population group. Finally, we must keep in mind that the earlier in life adults quit smoking, the greater the positive impact on public health.

Thank you for your attention.

DR. SAMET: Thank you.

Questions? Neal?

DR. BENOWITZ: It seems like the results of your survey are a little bit different from some of the other ones, like, for example, the NSDUH.

MS. HARTMAN: I don't believe they have ever asked this question.

DR. BENOWITZ: Right. In terms of age trends and prevalence and whatnot.

MS. HARTMAN: Oh, you're talking about the percentage of current smokers that smoke menthol cigarettes?

DR. BENOWITZ: Yes. And so I'd just like to know what you think the important differences in the methods are in terms of populations who are accessed through the questions. I'm just trying to get a sense -- I'm trying to reconcile the --

MS. HARTMAN: Okay. I guess it would help maybe if you said that because my understanding is that they're about 30 percent in the general population and somewhere between 70 and 80 percent in the non-Hispanic black population.

DR. BENOWITZ: Is that right? I'm not sure.

DR. SAMET: But, Neal, there was some discussion you probably heard about the age gradients and menthol use, which I think you showed a fairly -- why don't you go back to the slide, and perhaps that

will be one of the points I think Neal was referring to.

MS. HARTMAN: Table 1? This one?

DR. SAMET: Yes. So I think, if you heard the discussion earlier, there was some discussion about the extent to which such gradients exist. And here there's a very clear and strong gradient in age.

MS. HARTMAN: Yes. Menthol use seemed to decrease with age.

DR. SAMET: Right.

DR. BENOWITZ: And so could you just follow up in terms of the report?

MS. HARTMAN: Oh, this is not a longitudinal. This is cross-sectional.

DR. BENOWITZ: Right. We understand. And so when you got menthol, what question did you ask? Did you ask, do you smoke menthol or not? Did you ask for brands? Do we know what --

MS. HARTMAN: No. We asked, "Do you usually smoke menthol or non-menthol cigarettes?"

DR. SAMET: Okay. Dan?

DR. HECK: I was just going to observe, in

seeing this for the first time, it looks like these percentages here are percentages of smokers. Right?

MS. HARTMAN: Oh, yes.

DR. HECK: Not percentages of population. There may be some confusion.

MS. HARTMAN: Oh, yes. Yes. As I said, this was asked of current cigarette smokers. Oh, definitely.

DR. SAMET: Other questions or comments? So if you might say one thing. This was from the first three months of data collection. There'll be further data forthcoming that might give a more robust sample, or --

MS. HARTMAN: Yes. For this, though, this is 10,000, which is a really large sample. I think that the best thing would be that the second question is based on about 3,000. And the reason I also didn't go into other subgroups is because I didn't want to get much smaller, although these kind of differences are likely to be significant.

DR. SAMET: Other questions from the committee? Yes, Tim?

DR. MCAFEE: A quick question as to whether -- I completely agree with your statement that behavioral intent is associated with actual behavior. But I'm curious if you have any thoughts of ways that you think before the fact, i.e., in our current state of the status quo, any ways that we could try to use this data to come up with a quantitative estimate for how many people, as a result of a policy change, would actually, A, make a quit attempt, and B, be successful.

MS. HARTMAN: That's a good question. I'm a biostatistician. However, my colleagues, who are experts in behavioral research, cite literature supporting the conclusion that behavioral intention is associated with actual behavior. So there may be others who would be better to give you the answer to your question specifically, like what percentage would you expect of the, say, 39 percent would actually quit? I don't have that.

DR. MCAFEE: Thanks.

DR. SAMET: Okay. Thank you for your presentation.

We'll move on. Our next presenter is Jeannette Noltenius with the National Latino Tobacco Control Network.

DR. NOLTENIUS: Good afternoon. I'm Jeannette Noltenius with the National Latino Tobacco Control Network, and I want to thank you very much for the opportunity to address you.

I am just going to talk about -- in terms of disclosure, I have not received any funds from the tobacco industry to be here. Secondly, I want to say that I am just speaking in terms of what you all are doing as a reaction from the community, not as a scientist.

First of all, in terms of the community perspective, we're talking about a product that signifies 30 percent of the market. Okay? And so if you look at, after you do your deliberations, how the community is going to react to this, this is -- yes, it is 30 percent of the market. And what would happen if that market share would be eliminated? There's an impact there, with the community seeing that the FDA is truly protecting that community,

especially when we're talking about such high rates of smoking mentholated cigarettes in African Americans.

By the way, 60 to 65 percent of Native Hawaiians and Pacific Islanders are also menthol smokers, and 37 percent of Latino women are menthol smokers. So you're dealing with a situation in which this issue is affecting communities of color.

I want to say that it's an issue that is going to impact not only how we perceive regulations to be and how willing communities are to engage in tobacco control, but also we're concerned about the fact that it's already proven that this is a starter cigarette, that mentholated products is a way in which adolescents start to smoke.

Ergo, it is a way in which menthol helps the poison go down. That's how the community reads it. All of the scientific literature has its different perspective, but that's how the community can read this. Therefore, it makes it easier for young people to start smoking.

It's important that you see that because that

is what goes on at the community and how the community sees it. Therefore, the National Network, the National Latino Tobacco Control Network, representing 2,500 Latino advocates around the country, feel very much that banning of menthol is important.

Another thing that I just want to mention and that I've seen all day long today and in previous meetings, the issue of data. We're using a lot of national studies.

DR. SAMET: Sorry, your time is up.

DR. NOLTENIUS: My time is up?

DR. SAMET: Yes.

DR. NOLTENIUS: All right. Thank you very much.

DR. SAMET: Okay. Thank you.

Questions? Yes, Dorothy?

DR. HATSUKAMI: I'm curious to know, if there were a ban on menthol cigarettes, what kind of educational programs do you think would be necessary to inform a community like the Latino committee?

DR. NOLTENIUS: Well, I think serious

educational efforts. I mean efforts in which you're talking about the product. You're talking about the impact of smoking that product. Those educational efforts, as you know, have been going down through the years. Right now, many states are not doing a lot of the prevention and education methods. And so you have to go down to the community level. You've got to be supportive of community-based organizations. It has to come down, really, to grass roots.

It's like what we've seen in terms of the retailers. Yes, the retailers at the community level are going to be impacted indeed. Okay? And we have had testimony from them, but at that local level in the schools, in the churches, at the community?

I think that there's a rare opportunity here to go down and really explain how these products work, and the fact that they have a public health impact, that they are limiting the number of years of life among people. So it's a great opportunity for the FDA. And it's a great opportunity for all of you to think that science is there in favor of humankind.

That is the true purpose of the scientific development process.

DR. SAMET: Mark?

DR. CLANTON: In your opinion and based on your experience, if there were no ban on menthol, however there were a ban on marketing menthol cigarettes, what would the reaction of the Latino community be? Would they continue to buy mentholated cigarettes if there were no marketing of those cigarettes?

DR. NOLTENIUS: We'll probably restrict -- I mean, we're in the guessing game right now, and I will be saying that I'm guessing. But Latinos are very brand-loyal customers. So the smokers that are smoking menthol very likely will continue smoking menthol if they're adults.

But the issue is, how do we then stop the marketing, which is specifically marketing to Latino communities, to African American communities, to poor communities. I mean, we've proven that. So if that stops, okay, we may see some reaction and positive. But I think that the best solution is to actually ban

it completely, and then we shall see. But that's a step that I would consider the reasonable step to take.

DR. SAMET: Okay. Thank you for your presentation.

Next we have Ellen Vargyas from Legacy.

MS. VARGYAS: Thank you. My name is Ellen Vargyas. I'm general counsel at the American Legacy Foundation, and I very much appreciate the opportunity to be here and address TPSAC.

As a lawyer, not a scientist, I am going to ask for your indulgence to suggest that you think about some of these very important scientific issues in the regulatory and global context in which they are presented to the committee, particularly based on what Congress has enacted as the public health standard, which guides the issuance of a tobacco product standard.

In a submission, a detailed submission, that we've made to the committee, we go through this in detail. And with my scientific colleagues -- Dr. David Abrams, who is here; Dr. Andrea Villanti --

we have analyzed the scientific evidence. But I'd like to just, in these few moments, highlight what I believe is the appropriate framework.

Specifically, it is our view that a tobacco product standard banning menthol would be appropriate for the protection of the public health. There would likely be lower levels of smoking initiation and higher levels of smoking cessation as a result of such a standard.

Particularly important in terms of looking at the framework is the issue that some have suggested; and some who I've heard speaking earlier today would have you answer a question that the statute does not ask. They would have you answer the question as to whether it has been proven that menthol causes -- and I believe Mr. True spoke earlier about causation -- an increase in adverse health effects to established smokers, but that's not the question that the statute asks.

The question -- the statute, excuse me -- asks you to weigh likelihoods, risks, and benefit; specifically, likelihoods that a standard, in this

case a ban on menthol, would result in lower rates of initiation, particularly among youth and particularly among the youngest youth who we know are the most likely to smoke menthol, and the likelihood of whether a tobacco product standard banning menthol would result in higher rates of cessation. And we explain in detail why we think both effects are likely. And I am here, again, to emphasize the question that is before you and to respectfully submit that that is the question on which you should focus.

Finally, just a quick word on risks and benefits. The statute also asks you to weigh risks and benefits, and regulatory law makes it quite clear that you look at the risks and benefits in light of each other.

So, for example, when you're looking at risks and benefits to nonsmokers, overwhelmingly youth, there are no risks whatsoever to nonsmokers, to the 12- and 13-year-old who has not yet started to smoke.

DR. SAMET: Sorry. Your time is up. Please.

MS. VARGYAS: Thank you. I'd be happy to

answer any questions.

DR. SAMET: Thank you.

Tim?

DR. MCAFEE: Well, actually, I was going to ask you a question about where you were just going with this. I'm curious what your thinking is. There's been a strong case that's been presented by a number of people from different positions that, in fact, there is a danger for youth, and that that danger for youth is related to contraband, the black market, et cetera.

What is your analysis as to why that is or isn't a problem for youth?

MS. VARGYAS: Well, I think we come at it from the point of view that 80 percent of smokers start before the age of 18. Over half of lifetime smokers of existing cigarettes will die prematurely from smoking cigarettes.

I think, honestly, it's a little disingenuous to suggest that a ban on menthol is going to create youth smoking problem. We already have an enormous youth smoking problem. Any young person who wants

can find cigarettes, can smoke cigarettes, and that's who starts to smoke cigarettes.

So we've been looking -- I understand, at a previous meeting, some of the industry representatives had said they were going to post studies looking at the contraband issue in supporting their position that additional amounts of contraband would be a real problem. We haven't seen that posted.

From our sense, in the absence of that evidence, I think that much of what is being presented is speculative. We're not suggesting that there would be no contraband problem, but we do suggest that it is critical to look at it in terms of what we know, which is any teenager who wants, just about, can find cigarettes to smoke. So the fact that there may be contraband cigarettes out there I don't think is going to particularly change that equation.

We also believe -- there's studies that are out there -- that the manufacturers of cigarettes have a great deal of control in the distribution of

their product in terms of the extent of contraband. We would note in particular that the largest manufacturer of menthol cigarettes, in this case Lorillard, in certainly its public statements says that it manufactures all of its products in the United States. We would think that they will have a lot of control over the distribution of contraband products, and we hope that they would step up.

DR. MCAFEE: Thank you.

DR. SAMET: Other questions from the committee? Neal?

DR. BENOWITZ: In the report from Ms. Foster, it talks about the idea of providing an adequate advanced notice of a ban and assuring cessation services of treatments. And, again, that's not something we've talked about.

I just wanted to know, can you expand a little bit about what you think would be the optimal way to transition if menthol was banned?

MS. VARGYAS: Certainly. Thank you for asking that question.

We note, certainly in the legislative history

where there's a concern expressed, and I think the language that is used is "sudden and precipitous" withdrawal of a product to which so many people are addicted from the market. And we think Congress's concern was appropriate, and we share that concern.

We think that the best way to go is to give some period of notice to people so that the product doesn't disappear from the shelves the next day or the next week, but within a reasonable period of time -- six months or a year -- that people can have that notice. And we think that that should be accompanied by a public education campaign and the stepped-up provision of cessation services.

Now, this can be through advertising. Excuse me. Quit lines. There's a growth of web-based resources which are increasingly helpful in assisting people quit smoking. A great deal of this is public education in terms of trying to educate people about how to quit smoking.

My organization, Legacy, of course, is actively involved in that market, and we have done a great deal of research on how to help people, through

public education campaigns, learn how to quit and how to access services. Of course, there are others out there in this space as well who can do a good job.

But we would suggest that a ban be, as I said, six months, a year, in the future so that people have that information, and that it be accompanied by a robust public education campaign which provides real information and links to cessation services.

There's a great evidence base about how to help people quit, and I would strongly urge that this committee and the FDA take advantage of that evidence base of services and make those available to menthol smokers, and others, who hopefully would also feel some -- would get some benefit from that.

DR. SAMET: Okay. Any other questions?

[No response.]

DR. SAMET: Thank you.

MS. VARGYAS: Thank you.

DR. SAMET: Then let me just make sure before we end the public session, we had one person signed up, the first speaker, George Della, who I think is

not here?

[No response.]

DR. SAMET: Okay. Then this ends -- the open public hearing portion of the meeting is now concluded and we will no longer take comments from the audience. The committee will now turn its attention to address the task at hand, the careful consideration of the data before the committee, as well as the public comments.

Actually, I'm going to suggest that the committee first turn its attention to taking a 10-minute break and recharging, then, we'll come back. So why don't we come back and get started at 4:00. And thanks to the public for your comments.

(Whereupon, a recess was taken.)

Committee Discussion

DR. SAMET: During the break, we had some discussion about schedules, concern about the weather tomorrow, and whether -- whether, w-h-e-t-h-e-r -- there's the possibility of missing flights or other things tomorrow.

So what we've decided to do, and especially

since we're running ahead, is to do a little of tomorrow's work today, with the possibility that hopefully we could finish up earlier enough that those who need to go can get out of here tomorrow before storms arrive, a storm arrives, if it does.

So what I think we're going to do, then, is first return to the topic that we've been discussing and the comments from the public hearing. I think we need to discuss the discussions of contraband and the broad picture that we heard and think about implications for our report and our handling of this topic. We heard interesting new data from the TUS and other things.

Then, what I would propose is that we move on and discuss the draft of chapters 1 and 2, the substance, much of the substance of which we have already discussed as a committee. But I think this is clearly a moment in time where we need to be, I think, very much in agreement with the methods that we have selected for approach. We're also going to hear from, I think, Dan concerning the industry report, representative report, that's being prepared.

So let me first turn us back, then, to the topic of the afternoon, the presentation by Michael Hering and our public comments, and suggest that we focus on those issues for a while. So let me do that.

Neal?

DR. BENOWITZ: I have a question about the self-mentholation. I assume menthol is widely available and is legal and is cheap. Right? That's not something that's banned or controlled in any way.

Is that right?

DR. HUSTEN: My understanding is you can buy menthol oil or menthol crystals.

DR. BENOWITZ: Okay. So if someone wanted to mentholate cigarettes, instead of doing it illegally or black market, they could just spend three bucks and buy some crystals and throw it in the bag.

Is that right? Is that people's impression?

DR. SAMET: Well, yes. Dan, you can comment. But wasn't that the original origins of menthol cigarettes?

DR. HECK: Yes. In fact, it was. And, Neal,

your sense is correct. It is very easy in a contained space for menthol -- or, in the case of the contraband, perhaps something that smells like menthol -- to partition into tobacco overnight or in a short period of time. And, as we've heard today, in essence, that method is used commercially as well as a direct spray application.

DR. BENOWITZ: I guess from my point of view, I guess because it's naive, but if you can do something that's so cheap and so inexpensive, why would you spend a lot of money and why would you break the law and get black market cigarettes? I'm not sure the problem is going to be as big as people said it might be.

DR. SAMET: Mark?

DR. CLANTON: I think the time and effort that would come along with a person mentholating their own cigarettes is important. If you look at the marketing model of the industry, tobacco is found almost anywhere you can buy any other product. It is almost universally available in this country. And that implies convenience is important to sales and

sales volume. So I think that a barrier of having to mentholate your own cigarette is probably going to allow some people to engage other options, if that's the only option that's available to them.

DR. SAMET: Jack?

DR. HENNINGFIELD: I think all of these discussions about options and how much more difficult it would be really go back to something I raised earlier, which is the need for modeling under different scenarios with different distribution. Because it's not just, can you do something, but what is the cost?

Again, we know this from cigarette marketing. We know it from illicit drugs. We know it from many species. If something is less available, costs more, you have to work more, it decreases intake. It doesn't mean that somebody won't do something crazy to do it or there won't be a subpopulation. But we've heard some very disparate scenarios, and yet from Legacy, we also heard about the large numbers of people that would intend to quit.

Again, that doesn't mean all those people are

going to actually do it. But I think some modeling as to various scenarios -- for example, if menthol was banned, part of the modeling in the scenario would be, what is the education communication?

Presumably the public would be warned very seriously against maybe harming yourself further. An industry representative mentioned earlier today that contraband might be more toxic. Those kinds of messages may also discourage people from seeking contraband cigarettes.

DR. SAMET: I think, in terms of thinking about our report, to sort of bring us back to our original diagram from July, David Mendez's representation, I think, of the same process, and think about chapter 7, which is the public health impact chapter, which I think we have conceptualized a number of indicators. Some of this is in the chapter 1 and 2 discussion of the consequences of having menthol in cigarettes.

What we have not done is, let's say, built off a number of sub-models, if you will, or alternatives of things that could happen, let's say,

if menthol were no longer present in cigarettes. We've heard some of those. There could be a larger black market. There could be access to counterfeit cigarettes, which perhaps would have higher levels of toxic contaminants. Criminal activity might be increased. Tax revenues would decline because of the presence of a black market with other consequences, and so on.

I think we've heard, among other things in the public presentations today, probably a pretty thorough listing of what some of those are. I think what we need to talk about here is how we're going to handle them in our chapter 7. I think they all need mention, and I think we can acknowledge that there are possibilities. It sounds like there's a powerful experience in Canada, for example, that needs mention. We heard from one group of economists with one set of scenarios leading to a particular set of results.

So I think we need to look at this information. Being realistic about time, I don't see that we're going to go build a model of black markets

or anything else. So I think the question of how we fold these into our report needs some discussion.

Then perhaps, Corinne, I need a reminder on what we were doing where we said we needed additional expertise on the question of contraband, whether we have somebody particular brought on for that or we've had the presentation by Michael, and you might remind me of that.

DR. HUSTEN: I don't recall that the committee gave us a specific name of an expert that they wanted.

Caryn, do you? I don't remember. I mean, there was a general talk about perhaps needing that expertise, but we asked each of the writing groups to let us know people that they would want, and I don't believe any names came forward or specific requests came forward on that. So part of our attempt to address this was to have a presentation today.

DR. SAMET: Mark?

DR. CLANTON: Well, in chapter 7 we did recommend one expert, so I'll ask some additional questions about whether that was acted upon or not.

DR. SAMET: It's probably getting a little late in the day, I suspect, to bring on somebody. But we can perhaps hear from you about whether that's realistic, if we have identified someone who might be helpful on these issue.

Yes, Jack?

DR. HENNINGFIELD: On the topic of modeling under different scenarios, I'm not sure that that's needed for this report. I think that's more something that would be needed to help FDA manage whatever they decided to do.

Frankly, right now FDA in its CDER, its drug division, has a lot of experience with what's called risk management, which is assessing various risks under various conditions and then coming up with what strategies you need to mitigate the risks and detect them quickly if they occur and intervene if that's necessary. So I really don't think this is something that we need to have in the near term.

DR. SAMET: So you're suggesting that if there were to be a ban, that in a sense there's a need for both surveillance and potentially for

modeling of what could be consequences.

DR. HENNINGFIELD: Yes. That would be, I think, where again FDA's CDER division does this increasingly routinely with other drugs, especially addictive drugs, where the concerns have to do with diversion, with young people using them, which is to identify all potential adverse scenarios and risks, come up with a plan to minimize them, et cetera, et cetera.

DR. SAMET: Other comments on these points or any other aspects of what we heard from the public? Yes, Melanie?

DR. WAKEFIELD: I suppose, just following up from the presentation earlier on today, I just wanted to get clear on the distinction between cigarettes and little cigars because there were a couple of different definitions thrown around, and I think it's important for us to be clear about it.

One definition was that little cigars are basically cigarettes, but they're wrapped in paper which is infused with some form of tobacco. Another definition, or an additional element to a definition,

is that little cigars are -- the definition is really consumer-based, so that it's really what consumers think they are or expect them to be.

Does anyone know, and who defines it?

DR. HUSTEN: Well, there is a definition of little cigars in the statute that does include an aspect that the consumers perceive and use like cigarettes. I don't know that that's been operationalized into how you would determine that.

Go ahead.

DR. SAMET: Arnold?

MR. HAMM: Yes. I believe TTB has a physical definition of a little cigar.

DR. WAKEFIELD: What's TTB? Sorry.

MR. HAMM: Tobacco Tax --

DR. LAUTERBACH: Tobacco Trade Bureau.

MR. HAMM: Yes. They have a description of -- a physical description of a little cigar.

DR. SAMET: I think it would be useful for us to have clarity.

Tim?

DR. MCAFEE: Well, I just had a quick follow-

up on that, partly to Jack. It's sort of whether -- because certainly one of my take-aways from this, which I was more dramatically impressed with than I had been previously, was that the issue of how -- that there's certainly the issue of contraband, but there's also the issue of this essentially legal mechanism by which menthol use could be sustained, which almost could make, from a public health perspective, a decision to ban it in cigarettes marginal, assuming that we came to the conclusion that, oh, this would have a public health benefit, that this would be marginalized by this fairly straightforward tactic that could be employed.

So I guess my question is, is that something -- Jack, would you see us turfing that to FDA or is that something where, at a minimum, we should make a recommendation? And I guess I'm probably advocating that, at a minimum, we might think about, if we got to that point, that we should include information about this loophole, essentially, and the need to address these concurrently, not just wait for it to happen.

[Dr. Henningfield nods affirmatively.]

DR. SAMET: That's a yes?

DR. HENNINGFIELD: Yes. I think it's a loophole that has to be addressed, whether it can be addressed within the statute or if it needs some modification. But, I mean, the intent of the law is clearly to address cigarettes. And if there is a clever way of just getting around that, that defeats the intent of the law.

DR. SAMET: Okay. Other comments about this afternoon, the contraband or the risks issues? Yes, Tim?

DR. MCAFEE: Well, we got a lot of information. I would just make a follow-up comment relating to the testimony that we heard from NCI relating to the intent of smokers if menthol were removed, which I actually thought was in some ways the most new information that we have, because as was pointed out, ultimately our charge is more related to what would be the public health impact of a ban than it is necessarily what's currently going on, what went on in the past, et cetera.

Our real concern is what would happen if this were done, and this was really the first straightforward information that we'd gotten as to what the intent of smokers would be. And the numbers were actually a little higher than I would have anticipated.

My back-of-the-envelope one, which I was asking the question, would be, well, what we know is that about 60 percent of smokers, as a class, say that they're intending to quit over the next year; and of those, more than 40 percent make a very substantial quit attempt. You know, 40-plus percent of them quit for more than 24 hours.

So I would say this is new information that might suggest that a substantial fraction of menthol users would make a serious quit attempt. And what we really don't know is how many of them would be successful and whether it would be a one-time phenomenon or if it would increase the probability of them making quit attempts over time.

But these are things that -- I guess one of my questions that I think we should think about, both

in the short run between now and March, if there were any way to get more information along these lines, it would be extremely useful to us, or even if there are analog, for modeling purposes, ways to get more specific around that.

I think it also ties to Dorothy's question about a public campaign. I suspect that the number of people that would actually act on their intention, this is not an immutable number. It's something that would be influenced by how it was rolled out, and it would be influenced by the communication campaigns that were given, resources that were made, et cetera.

DR. SAMET: I would actually see this almost as the flip side of the discussion we had about risks, that if, again, there were to be a ban, that it's in fact an opportunity to increase public health impact because of the kinds of information that, for example, we were just presented with, that there might be more individuals or a substantial population or individuals who might make a quit attempt. And then, perhaps with appropriate education, interventions, and so on, there could be a

substantial increment in the number of quitters. This would seem to me to be something else thought we would, for example, fold into our chapter 7 discussions, conclusion pending, which of course is not by any means reached yet.

Just to edify everyone as to what a little cigar is, here it is from the Act. "The term 'little cigar' means a product that is a tobacco product," and then, "meets the definition of the term 'little cigar' in Section 3.7 of the Federal Cigarette Labeling and Advertising Act."

So whatever that is, if, Corinne, you happen to know that and can quote that --

DR. HUSTEN: Well, I don't have that. But the definition of a cigarette is, "A product that's a tobacco product and meets the definition of a cigarette under FCLAA." But then there's a part B that says, "includes tobacco in any form that is functional in the product which, because of its appearance, the type of tobacco used in the filler, or its packaging and labeling, is likely to be offered to or purchased by consumers as a cigarette

or as roll-your-own tobacco."

DR. SAMET: Okay. Now that we've cleared that up --

[Laughter.]

DR. SAMET: Anything else on these topics? Mark?

DR. CLANTON: I have a question for Neal. Normally, when you do mechanistic studies for drugs, you don't have to do a population-based study. You know, you basically work out if a drug hit certain targets or certain metabolic functions happen on a regular basis when some intervention happens.

So on these few data having to do with how menthol affects nicotine metabolism, at what point would you be satisfied that there's enough mechanistic data about menthol slowing down cytochrome or P450 metabolism? I mean, how much data do we need to begin to make population-based conclusions about what's going on there?

Again, I bring that up because we know in African Americans in other drugs and in other cytochrome systems, they do metabolize at a slower

rate, a number of drugs. And this may be relevant to why African Americans may smoke fewer cigarettes but in fact may be more addicted.

DR. BENOWITZ: There is a database that's broader. There's only one human study, which was one that I published. But there also are studies in liver microsomes, one published study and one unpublished study, showing that nicotine inhibits menthol metabolism in microsomes. And her study in humans, while it's a small study, was certainly consistent with that.

On the other hand, the effect was relatively small. African Americans have a number of CYP2A6 variants that are associated with slower metabolisms. So their metabolism is slower by 30 percent, on average, compared to whites, but that's mostly due to the other variants rather than the menthol effect.

So we saw the effect in African Americans when they were not smoking, and we just basically gave them infusions of nicotine when they weren't smoking. So there's a couple reasons why African Americans are slower metabolizers. One is the

menthol, but the other is just genetic variance.

So I'm pretty confident that that phenomenon is real. But how important it is, it's a relatively small effect. It was like 10 or 15 percent.

DR. SAMET: I have one other comment, Mark, that I thought was part of your question, which is, how do you know when you have enough evidence to have identified a mechanism? And a bunch of us around the table were involved in the recent surgeon general's report, which had the topic, as I mentioned, of the mechanisms by which smoking causes disease.

There's a chapter 1, which I also had a hand in partially writing with Dave Sidransky, where we tried to write about this issue. And, in fact, it's interesting because as much as we talk about identifying mechanisms and we have a lot of approaches for causal inference, there's been less thinking about how one knows that they have identified a mechanism, or EPA talks about broader things like mode of action, where they use so-called weight of evidence approaches, which I think means a bunch of people sit around a table, largely, and say,

well, there's enough evidence here.

But I think there's some discussion of this topic in general. And in that report, the conclusions around mechanisms were couched in a way that expressed some feeling for the level of certainty that a mechanism had been identified. And it's probably a potentially useful approach that we can remind ourselves of for our own tasks, and probably there's some nuggets buried in that report that would be useful for all. And it's available online in all of its, whatever, 6- or 700 pages.

Yes, Dan?

DR. HECK: Yes. I was going to try to address Mark's comment, but Neal did a good job, I think, of touching on most of those topics.

It seems like a long time ago now, but we may recall from an early TPSAC a submission that some of the industry research scientists at Lorillard submitted looking at the cytochrome P450 activity and its potential inhibition by menthol, and kind of confirming what the MacDougall paper with S9, I think that Neal was referring to, saw. And that is that

the potency of menthol in affecting this enzyme suggested, to us anyway, or to the scientists at Lorillard, that the levels that might plausibly be achieved in human smokers would be several orders of magnitude too low to have a meaningful effect.

I think we've seen its -- it was presented in July by Dr. Sarkar in his total exposure study or presentation. That very large study of almost 4,000 real smokers in the field smoking real cigarettes, looking at the metabolite ratio, both the glucuronidation pathway of interest and for the CYP2A6 pathway, there didn't seem to be any association of the altered metabolite ratios with the mentholation of their brand. So we have a lot of diverse and not entirely inconsistent information to consider on that question.

DR. SAMET: Okay. Any other comments on the topic of the afternoon?

[No response.]

DR. SAMET: Then let's switch gears and move on to the discussion of the various drafts. I think before we move into the main TPSAC report, Dan's

going to give an update on the report being drafted by the industry representatives. Dan?

DR. HECK: Thank you, Mr. Chairman.

The committee may recall that the FDA, I guess, disinvited the non-voting industry representatives from participating in the report-writing project, and the industry stakeholders were invited to prepare a separate report.

We are pursuing that. The intention will be to deliver that report on a similar time frame or identical time frame to that specified by the voting members. And the intention also will be to model the structure of that report broadly, similar or analogous to that offered by the voting members.

I don't know as I sit here today exactly which industry members may choose to sign onto that report. Certainly everyone will be offered an opportunity to do so and will have a chance to review and comment on the draft text when it's available. We'll have to figure out the mechanism for doing that in the next few weeks and months.

DR. SAMET: Questions?

[No response.]

Chapters 1 and 2 – Introduction and Evidence

Jonathan Samet

DR. SAMET: Okay. Thanks, Dan.

Then I think what we'll do is move on to a discussion of the draft chapters 1 and 2. So let's see. Maybe I'll go stand up. It just feels good to stand up.

Okay. So these two chapters are sort of foundational and are descriptive of what we're going to do and how we're going to do it. And we've actually along the way had substantial discussion about many of the components of what are here and the principles.

So I think what is critical today is we see if there's any more discussion and make certain that we are comfortable with the general approach that's been set out. This is work involving Mark, Dorothy, and myself, and at this point there's a relatively-far-along draft.

So this is a statement of what the chapters are about. First, it introduces the purpose of the

report. Provides our charge with regard to menthol. Describes the conceptual framework, which we've now seen since July, I think, when the first version of this was put together. And it sets out the general approach that we will be taking in preparing the report.

It describes the approach to classification of strength of evidence that we have now down side at some length, and as you remember, that was based around this idea of equipoise.

Now, first off, a statement on what our charge is, developing a report and recommendations -- so it's both -- that address the issue of the impact of the use of menthol in cigarettes. And, again, it's the impact of the use of menthol in cigarettes -- and just flipping the wording, not menthol cigarettes -- on the public health, including such use among -- and then the description of the various populations -- children, African Americans, Hispanics, and other racial and ethnic minorities. And this of course will be front and center in chapter 1.

Then this is the following they were charged with addressing under -- wow -- 907(a)(3)(B)(i), the risks and benefits to the population as a whole, including users and nonusers of tobacco products, and I think that's been a lot of where we have been today; the increased or decreased likelihood that existing users of tobacco products will stop using such products; and the increased or decreased likelihood that those who do not use tobacco products will start using such products, and this, again, having to do with the impact of menthol.

The framework, just as a reminder – and, again, this is somewhat parallel to the model that David showed -- has youth and adolescents, experimentation, initiation, menthol smokers, non-menthol smokers, addiction, cessation, continuation, again as the possibilities, and showing in the end that disease and premature death result.

We are concerned, of course, with the impact of marketing. There are multiple places where marketing may have a role. Melanie, I suspect I don't have all the arrows going to all the right

places yet, and help me get this straight. But there are a few more than there used to be.

So this model, in part, is similar to, in concept, what David showed us. I think what David actually did not have was this experimentation to initiation step. And if you remember, then, that was tied into a series of questions that we are addressing in our various chapters. And, again, here showing these linkages to how the various questions that we're answering figure into this framework.

So this was an attempt to tie into the conceptual framework these key questions that we are directed at, at the individual and population level. So, again, the questions were as follows. And I'll just run through them again. And remember, we intend, based on our reviews in chapters 3, 4, 5, and 6, to come back and provide answers to these questions on the strength of evidence available.

So likelihood of experimentation, likelihood of becoming a regular smoker, likelihood of becoming addicted increase the degree of addiction of the smoker. Are smokers of menthol cigarettes less

likely to quit successfully than smokers of non-menthol? Jack, I think these are roughly what you enumerated today around menthol and addiction.

Biomarker studies. Do they indicate that smokers of menthol studies receive greater doses of harmful agents per cigarette smoked? And, again, we had some discussion relevant to this question. And then this question of what the epidemiological studies show. Is there increased risk for disease that's caused by smoking in comparison with smokers of non-menthol cigarettes.

So these were our questions related to individual smokers, and then we have had two at the population level. Does availability of menthol cigarettes increase the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available -- the so-called counter-factual -- and in subgroups within the population? And then the marketing question, whether tobacco company marketing of menthol cigarettes increased the prevalence of smoking beyond the anticipated prevalence if such cigarettes are not available, and then again the

subgroups.

So those were the -- that's our charge, the questions that we have developed, and then the approach. And here, I think, we have the peer-reviewed literature, which we've seen a number of reviews already, including those carried out initially and presented to us by FDA; and our various chapter groups are working hard to identify essentially the universe of peer-reviewed literature relevant to these topics.

Beyond that, we have a number of other documents. Actually, I think this list probably should be extended. We have the industry submissions, as we heard about today. We have the selective review of industry documents. And, actually, I think we have now examples of ongoing analyses of data sets, another source that probably needs to be added to this list. So this list probably needs to be extended.

I think, in my mind, what's a little bit unique about it is here we can identify the universe of studies of interest. For the other sources, it's

a little more difficult. The industry submissions, we have those selected by the industry and submitted, and now reviewed by the various consultants brought on board to take a look at those.

We've had reviews of the legacy documents, again identified through the kind of selective snowball kinds of processes that are used to examine the documents. And we know that we cannot either identify or review the whole universe of such documents. And, in fact, what their contributions might be is not necessarily clear. But looking at this list here, I think we probably need to get it extended a little bit to include things like new survey analyses and other things that are being provided to us.

We have said that there are core principles that we intend to follow. We have some draft text not yet added to the chapter on this, that we will be evidence-based, and we are searching for the evidence. We will lay it out. We will be transparent in our approaches to identifying and reviewing the evidence and saying what we're looking

at. And then around classification of the evidence and looking at it, we will need to be consensus-based, and I think we might want to have some discussion about that point today.

Just a reminder that we spent a lot of time at our fall meeting talking about the classification of the strength of evidence. We talked about the concept of equipoise; that is, the strength of evidence hangs at the balance point as to whether a relationship is at least as likely as not.

Those outcomes for which the evidence is, more certain would fall into this top rank of strength of evidence. The evidence is sufficient to conclude that a relationship is more likely than not, and then a category of less likely, insufficient to conclude that a relationship is more likely than not, and there's insufficient evidence, so the bottom two categories.

Then we'll be using models. This is in part consistent with our charge, trying to meet our charge of understanding impact and that there are a number of potential indicators of impact, rates of

experimentation, initiation, progression of smoking, the rate of successful cessation, and risks for cigarette-caused morbidity and premature mortality. And, again, we're getting help from David Mendez with modeling that will provide us at least some estimates for some of these potential indicators.

Our job with the modeling is to, I think, work with David to provide guidance on whether we think that the model structures he proposes are those that we think are most consistent with how smoking occurs, addiction develops, and diseases are caused in individuals in the population. We will need to help him with what are the best estimates for various parameters in these models and describe scenarios that may be relevant.

I think that's all. So chapters 1 and 2 have a lot in them, and I think we'll just go ahead and discuss. So let me sit down.

Mark?

DR. CLANTON: Yes. I think the first bullet should be impact of menthol on various --

DR. SAMET: I'm sorry. This is menthol.

DR. CLANTON: Okay. I knew you knew. Now we all know.

DR. SAMET: I actually thought I'd fixed that once. I'm not sure. But this looks like the wrong set of slides. Okay. Thank you.

Yes?

DR. HENNINGFIELD: On the model, I thought we had discussed this, but the first box in the model, youth and adolescents, I thought we had expanded that to include young adults, because, especially, we see more people beginning smoking at 18, and I think that's more common in the African American community. So if the cutoff is 18, then we miss, potentially, an important intake.

DR. SAMET: So we should basically say youth, adolescents, and young adults in that model. Okay. For sure.

Dorothy, go ahead, and then we'll keep going back.

DR. HATSUKAMI: Yes. With regards to the questions, our chapter 5 group would like to request that the "access" be changed to "availability." So

if you can go to the slide that shows the questions that we're trying to answer.

The point was made that access really has a different meaning than availability. So I don't know where the questions are. But if we could do that, that would be -- we would appreciate that. It's number 1, the first question, 1 and 2. Question 1 and 2.

So for question 1, instead of, "Does access to menthol cigarettes increase the likelihood of experimentation," "Does availability of menthol cigarettes." And, secondly, "Does availability of menthol cigarettes increase the likelihood of becoming a regular smoker?"

DR. SAMET: Yes. Dorothy had brought this up, and since we had discussed these wordings earlier, I thought we should just make certain with everyone that the change from "access" to "availability" is fine with everyone.

Mark?

DR. CLANTON: I think it's a subtle distinction, but access can apply to almost anything.

In other words, can I take them from my parents' drawer, or can I appropriate them in various different ways? But availability, I think, is more of the marketing term in terms of the ability of people to get and buy cigarettes through normal marketing channels. So access may be too broad and availability, we think, is more specific to the marketing questions. That's the best explanation I can come up with about why one versus the other.

DR. SAMET: Melanie?

DR. WAKEFIELD: Yes. In our discussion, just to expand on Dorothy's point, I mean, access is often used for sales to minors issues, youth access and things like that. And it's a broader issue than that, so we felt that availability was more expansive and also pertained to marketing as well.

DR. SAMET: I don't think these are written in stone, our questions. So I think if the consensus of the group is – yes, we'll go to availability. All right. So we've changed Questions 1 and 2 to availability.

Okay. Melanie, there's your figure.

DR. WAKEFIELD: So thanks for putting "marketing" in, in the middle and at the end. But I think in the next slide, if you click forward, there will be a -- where you bring up these -- yes. So I'm not sure why that's in a different sort of --

DR. SAMET: So originally these were corresponding back to our questions, the numbers. They may not -- that was the -- that was why they were. But I think your general point is that number 1 should appear in a number of places besides where it is?

DR. WAKEFIELD: That's right. And, I mean, I would even -- just to be picky, I would say that "marketing" even applies in between "experimentation" and "initiation." I mean, I think one of the things we discussed is that some things apply all the way through. And I think we might have even talked in a previous call about having a kind of environmental box or something like that running along the bottom, of which marketing is one influence and other tobacco control policies and so forth are another. That's another way of thinking about it.

DR. SAMET: So marketing could potentially go in almost every transition?

DR. WAKEFIELD: It could, yes. Absolutely. And I think we're particularly charged to look at marketing here, so we probably should do that.

DR. SAMET: So let me ask, am I correct that where it says -- at least "parents, peers" might be at that first transition, but "marketing" could certainly go from continuing to smoke, cessation, et cetera, et cetera. So roughly, that 1, which is the marketing question, would apply everywhere, essentially?

DR. WAKEFIELD: Yes. I think so.

DR. SAMET: Okay.

Mark, in terms of these principles, you have the lead. Do you just want to say a few words about transparency, evidence-based, and consensus-based?

DR. CLANTON: I could if I remember what I wrote. I assume we're going to look at the text at some point. I do remember some comments about evidence. And I made further comments about, traditionally, panels like this only look at peer-

reviewed scientific information and evidence to make their deliberations.

I think I went on to say that when it comes to evidence as it relates to tobacco, the causes of initiation and the causes of persistence, success rates or failure rates in cessation are much more complex than what we might find just in the peer-reviewed literature. And there are other factors and issues that we may need to weigh outside of peer-reviewed literature.

We already know that we're going to be looking at documents and summaries of documents, which are not peer-reviewed. And so in order to accept that kind of information for analysis, we may need to look at other relevant information that is outside the scientific peer-reviewed literature in order to handle the complexity of why people start smoking, persist in smoking, and have difficulty stopping.

So I wanted to make that point in terms of the evidence and how we use the evidence. And I think, again, we may need to look at a more what's

called social networking or complex systems analysis of all of the evidence in order to understand it in the right context. And I made a few more comments about networking analysis and how those models might fit here.

Those are the things I remember that are relevant to the evidence and transparency. I think I may have made a couple of additional comments, but I'll have to look at them to remember what I said.

DR. SAMET: Neal?

DR. BENOWITZ: To follow up on that, I guess my question would be, what do we do about all the presentations that we've heard, all the PowerPoints and the NCI data, which was really provocative but has not been published? There's a lot of information that we've received that certainly is not published, and we need to have some kind of guidance for how to use it all.

DR. SAMET: Let's take the NCI data as an example. So here is new and potentially useful data, data that might be useful to inform models. And we've had a slide presentation. So I guess I have a

couple thoughts about it.

One is, for example, we could suggest that those data could be used in developing scenarios by David. I think it would be most useful that if we're going to rely on such data, we at least get a preliminary or draft report so we in fact have a document that describes the origins of the data, the analyses, and so on.

So, I mean, I think this is a good point. Would we rely on something presented only in slides where we don't have the core documentation? I suppose it comes from an agency that we know well and so on. But it seems the minimum is that there's some backup to the slide presentation that we have available. And I think maybe get a sense of how people around the table feel about that.

Neal?

DR. BENOWITZ: Well, what would we do, then, with tobacco industry documents where there is summary of results but we don't have the full data sets, for example? That would be an analogous situation. And certainly in the section I'm taking

the lead on, there are a lot of those things, talking about sensory research, where we don't have the data sets, but we have the results of the studies summarized.

DR. SAMET: So you've asked an unanswerable question, but one I think we'd better answer. Again, I guess I have the feeling that if knowledge has been generated by a survey or something else that we're going to use, that we should have some sort of tracking back of what it is and where it came from.

I think if somebody has summarized a wide range of documents, one of the contractors, that we are going to be left relying on those summaries because we can't redo it ourselves. But I think we can look for documentation of key information that's been generated through a survey that's perhaps not published or something else, recognizing that the TUS itself is well-documented. But I think for setting the standard, I think it would be useful to say that we have something.

Yes, Mark?

DR. CLANTON: I wanted to also say in the

draft, trying to clarify the principles, in addition to making it clear that we'll certainly focus on peer-reviewed data but we're going to be looking at other kinds of relevant data, I also made a point about randomized clinical trials.

In terms of looking for strict causality, obviously we would look through the peer-reviewed literature looking for randomized controlled trials. The truth is we're not going to find very many, and we're not going to find very many as it relates to important issues here.

So I wanted to make the point that if someone, whether outside or inside this group, only looks at randomized controlled trials as a legitimate way of understanding association, that, in fact, those data really don't exist in many cases. And we can certainly call for them, but we don't want to be crippled in coming to conclusions about the data because we don't have our randomized trials.

I also made a further point, and I'll probably need to expand on it, that a lot of what we're looking at, really it's perfectly appropriate

to look at cross-sectional epidemiologic studies. Those are the kind of studies where you don't necessarily get two controlled groups. A lot of what we're looking at isn't amenable to creating two carefully matched groups at all, but cross-sectional studies do allow you to look at non-matched groups. And, again, we don't want to cripple ourselves in any way by only thinking that RCTs are the only way of looking at association. And so, again, there was some language around that point.

DR. SAMET: Cathy?

DR. BACKINGER: Yes. Just getting back to talking about following up on presentations. So there were presentations made that were on the agenda and up front here, and then there were presentations that were made via the public. And there was a mix of both, data presentations on both sides.

So I guess it's not clear that if now -- and just a question: If you're going to ask for documentation or a written report, and to get the report done by March 23rd, are you all going to choose which ones you want to have more

documentation, for example? Because, again, there were -- I think it was July, and I can't remember; the months are blurring for me -- data-driven presentations from the tobacco industry for which you have their PowerPoints but you don't have reports.

So I guess just kind of wondering, back to Mark's question about transparency and evidence base, where do you draw the line and what are you exactly asking for, because I think that's a big bite to take.

DR. SAMET: I'm not sure there's a big bite that we're going to take. I think my suggestion is that those items that we regard as key or for which we're going to pull a particular number, that we might suggest as a parameter for models that we have very sufficient documentation of the origins of such numbers.

Certainly, on our time frame, we're not going to be going back and using every piece of information that we've heard between the various presentations. We've had a lot of input. And I think this is something that will have to hinge on the writing

groups' judgment as to something that may be particularly critical and for which we just really need to know where it came from.

Mark?

DR. CLANTON: From the beginning to the end of this process, given time constraints and other real-world constraints, I think we're going to make our best effort at writing this report and providing useful recommendations. I think, ultimately, transparency is going to be defined by disclosure. In other words, here's where -- these are the evidence that we used to come to Y conclusion. And whether we can create a perfect balance vetting all of the information, I don't know the answer to that. But at the very least, at a threshold level, transparency will be well-served by at least us making an identification of what we use and how we use it.

DR. SAMET: I wanted to spend a minute on this idea of consensus-based. Consensus is a pretty powerful word. This is a TPSAC report. It's being prepared by the Menthol Subcommittee, which includes

almost all of TPSAC. But it's a report of the group. It will do our job of providing a report and making recommendations.

From my perspective, the report should be, does need to be, consensus-based, which suggests that if there are issues where one or another committee members feels that if the group is here and they are perhaps here or there, that there needs to be sufficient discussion and airing of all those issues to make certain that the point of consensus seems to be the right one.

I think as we begin to answer these questions and use the evidence classification scheme, I can imagine the discussion -- well, gee, is this number 1, number 2, or 3, or 4, and so on. And those are often difficult judgments, and sometimes someone might see the strength of evidence as a category 1, and somebody sees it as category 2. It's probably -- we're at category 2, and some see it category 3, that it's also going to be a need for discussion. I think it would be naive not to recognize that categories 1 and 2, i.e., where the evidence is at least at

equipoise, may carry some decision-making, have some decision-making import.

So there's not, in a sense, room here for minority reports. We haven't talked about that, and what I see is that we have opened discussion about the evidence as we move forward with these chapters over the next two months, and that the process we're setting up -- and, again, I think we just all have to make sure we know what we're getting into here -- it says, well, the recommendations that come forward, the classification of the evidence, and so on, is TPSAC's collective judgment, which means we're all essentially signing onto those classifications and conclusions.

There are certainly many other examples of consensus-based reports. The National Research Council, the Institute of Medicine, typically has very few, if you will, minority reports. It's a question of discussing the evidence and also making sure that we understand where it is. I mean, I think disagreements can be useful because they bring out some of the difficulties in interpreting difficult

evidence. And we're certainly going to be confronted with various bodies of evidence that have gaps and uncertainties, and we're going to have to make these judgments. But I just want to make sure that we're all clear on what consensus-based is leading us to.

Dorothy?

DR. HATSUKAMI: Yes. I think it's really going to be critical for each of the chapters to describe the process by which they came to a consensus. And just as an example, our chapter in particular, we'll be looking at the number of peer-reviewed or number of studies that we have examined, the nature of the studies, as well as looking at the strengths and weaknesses of the various studies, and then coming to a consensus of where the evidence lies. So I think to make that transparent I think is going to be very critical as well.

DR. SAMET: Agree. And certainly that will help with consensus-building.

Other comments on this? Mark?

DR. CLANTON: I think a minority report of some sort could be problematic. I think we're being

requested by statute to produce a single report, the menthol report of this body. That doesn't mean that this won't be a complex process, and there may even be disagreement. But I think it would be better to reflect any legitimate disagreements in the body of the report and let the reader of the report come to their own conclusion. But I would almost argue from the very beginning to allow a minority report from us maybe fundamentally a bad idea.

DR. SAMET: Jack?

DR. HENNINGFIELD: I would agree with Mark, and be interested to hear FDA's comment. But it is a report for FDA. It isn't the final policy. We're not making the decision. So having an open process, discussing where there has been disagreement, I think serves FDA, on principle.

DR. SAMET: Well, I just want to make sure that we reach consensus about consensus.

[Laughter.]

DR. SAMET: Which I think we are. Any other thoughts about this? Any minority reports on consensus?

[No response.]

DR. SAMET: Okay. Well, I think it was important to make sure that we had that discussion.

Anything else? I think -- Tim?

DR. MCAFEE: This is just very quick. This probably goes without saying, but I would assume that literal consensus would be amongst the voting members. So that should be in the minutes, so to speak.

DR. SAMET: Yes. Okay. So we're still with chapters 1 and 2, which we are hoping to see come to a close soon. And I think we're pretty far along and close to doing that. And I think the discussion will be helpful in completing the writing, as will the long plane trip to L.A.

Tim?

DR. MCAFEE: I'm not exactly sure where this would go. But in reviewing your remarks, one of the things that -- in terms of something that we may not have quite built into the structure of this is essentially where we would put the data that was just presented from NCI, which really – because, really,

the way we've set up the questions both at the individual level and at the population level is all kind of a retrospective. It's all about does the fact that there's menthol in cigarettes now cause these things. There's nothing that says, does the availability or removal of menthol cigarettes increase or decrease the prevalence of smoking

DR. SAMET: Right. I think I said this. This would fit in very well in chapter 7. And I think there because that was where we were talking about the risks, potential risks and benefits. And I think the evidence would fit very well in a discussion there of, one, the potential consequence of, if there were a ban, that there would be this opportunity to help a large segment of the population stop smoking who would seem to want to under those circumstances.

Yes, Mark?

DR. CLANTON: I agree. That would fit nicely in 7. What we should mention and we didn't map out is that there are a number of these questions that are distributed in a repetitive fashion throughout

the chapters. So some of these questions you've asked actually be addressed by multiple chapters and various sections in those chapters.

So I wanted to mention that. That's important because in a sense, we all have a bit of the same assignment. We may come at it differently; marketing will come at it, Question 3 or whatever from a marketing perspective, and others might come at risk two or three times in several chapters.

So I wanted to make that point because that's relevant that these data, whether it's NCI or other data, may actually show up multiple times in the report because risk, I think, is going to be addressed at least by two chapters if not three.

DR. SAMET: Anything else on chapters 1 and 2?

[No response.]

DR. SAMET: Then, let's see. If we look at where we are, we're up to somewhere in -- tomorrow morning we have chapter 3, Neal, the physiological effects. Chapter 4 will take us between -- Patricia and Karen will do --

MS. DELEEUW: Yes. I think Patricia's going to do one.

DR. SAMET: Is Patricia planning on doing that through the -- okay. So Patricia will do that through the distance presentation. Dorothy and team have much to say.

Chapter 6 is really not started yet, but I think what we're going to do there is relatively straightforward. And, Mark, chapter 7 is somewhat promissory at this point but you could address general approach.

DR. CLANTON: Well, we have an outline and it's important for me to make this comment. There are two sections in chapter 7 that I think will represent original pieces. The issue on contraband needs to stand alone and probably won't be addressed, I don't think, by most other chapters. So contraband is going to be sort of an original section.

There's another section on health outcome, menthol versus non-menthol, where, again, that may be mostly original information that may not be pulled from other chapters. The other sections, actually,

are going to rely heavily on what comes from chapters 1, 2, 3, 4, 5, and 6. They may be synthetic pieces where we summarize conclusions and data from previous chapters.

So we have an outline right now to work from. But I want to make it clear that several of the sections in chapter 7 are going to rely very heavily on what comes from other chapters because it's about summation and synthesis of information, except for contraband and health outcomes, which we're going to write to stand on their own merit based on the evidence.

Adjournment

DR. SAMET: And I think perhaps recognizing that it's, what, January 10th, meaning that March 23rd is fast approaching and we can only do what we can do, it is possible that chapter 7 might also be a place in which we make some suggestions for further work that can be done and so on.

Okay. So let me ask if there's anything else. I think we're probably roughly ready to adjourn for the day, getting back together tomorrow.

We'll plan on starting promptly at 8:00.

So I want to thank everybody for their attention and hard work today. Hang in for another day. We'll do it tomorrow and see if we can't finish up early enough to beat whatever storm may come. So thank you.

(Whereupon, at 5:16 p.m., the meeting was adjourned.)